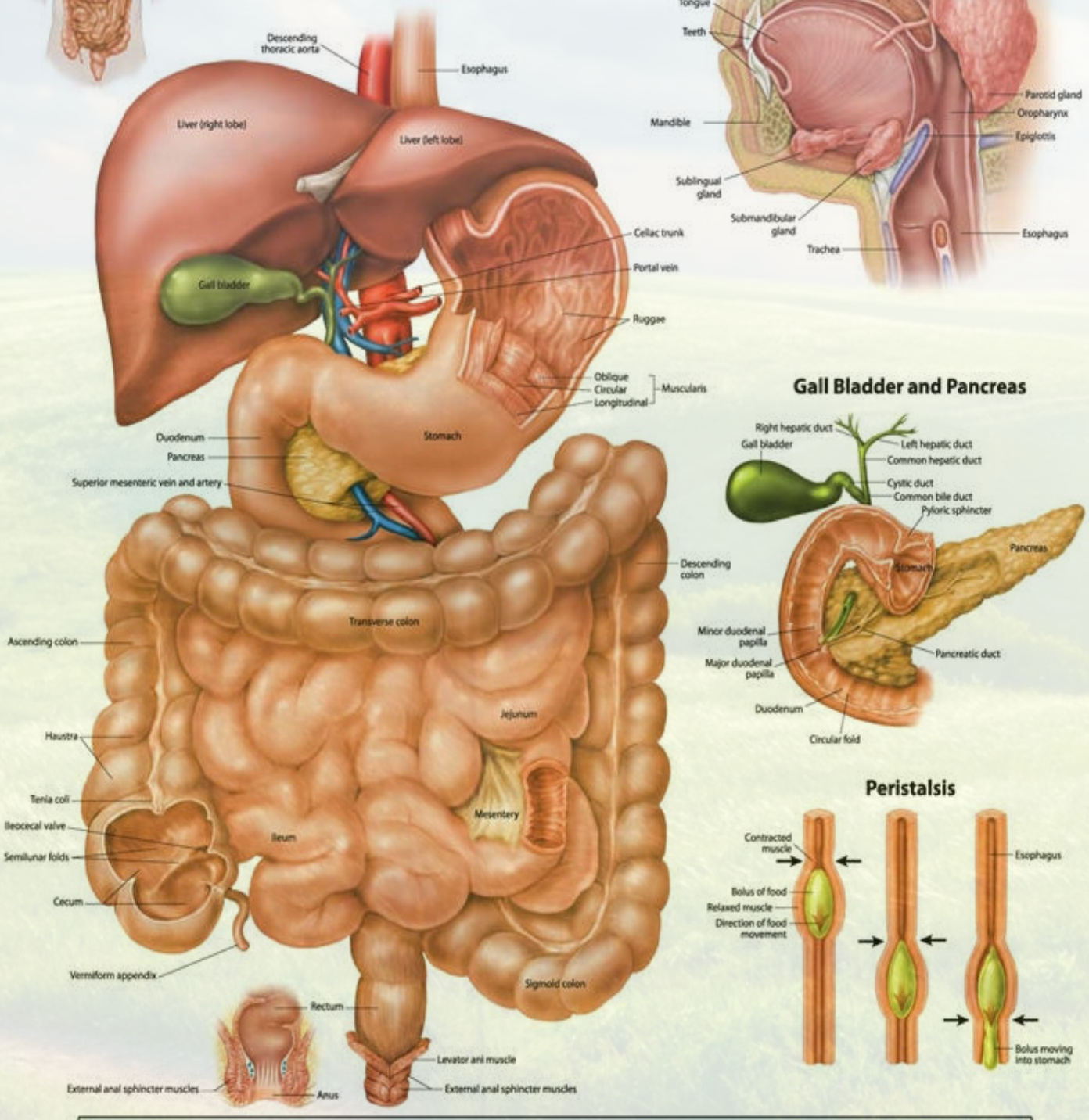
THE DIGESTIVE SYSTEM

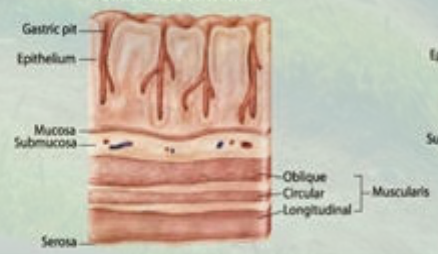


Oral Cavity

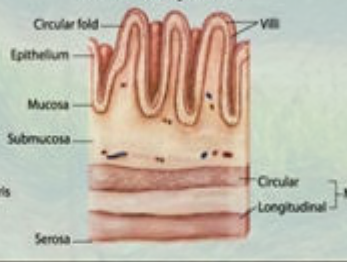
Gall Bladder and Pancreas

Peristalsis

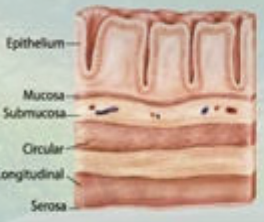
Wall of Stomach



Wall of Jejunum



Wall of Colon



INDEX

Refer to "Surgery" in:

- Portal Hypertension
- Peptic ulcer
- Pancreatitis

LIVER CIRRHOSIS

DEFINITION

- DIFFUSE Chronic liver disease characterized by:

  1. ***Degeneration.***
  2. ***Fibrosis.***
  3. ***Regeneration nodules.***
  4. ***Loss of normal structure:*** **IRREVERSIBLE.**

PATHOGENESIS

1. Hepatocellular necrosis leads to damage of the hepatic parenchyma & ***Degeneration***.
2. Excessive ***Fibrosis*** occurs due to excessive proliferation of connective tissue, why ?
   Injury of hepatic parenchyma → activation of stellate cell → +++ secretion of **TGF-β_1**.
3. ***Regeneration nodules***: will be formed.
4. ***Loss of the normal hepatic structure:*** IRREVERSIBLE.

   The liver may be initially ***enlarged***, but with progression of the disease, it ***shrinks***

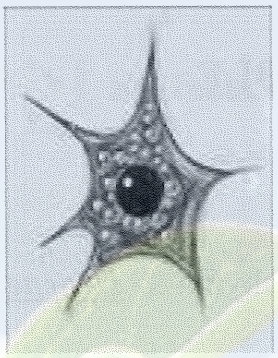
5. **COMPLICATIONS:**
   - Liver cell failure: due to progressive deterioration of liver functions.
   - Portal HTN: the fibrous septa will block the portal flow of blood through the liver
   - HCC: may occur.

CLASSIFICATION

1. Morphological classification: *micronodular*, *macronodular*, *mixed*.
2. Etiological classification: see the *etiology*.
3. Functional classification: *compensated* & *decompensated cirrhosis*.
4. Child's classification: for grading the *severity of cirrhosis*.

PATHOGENESIS OF LIVER CIRRHOSIS

Hepatic injury

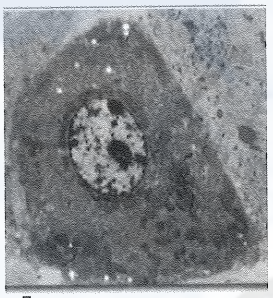


Activated stellate cell

TGF-ß1

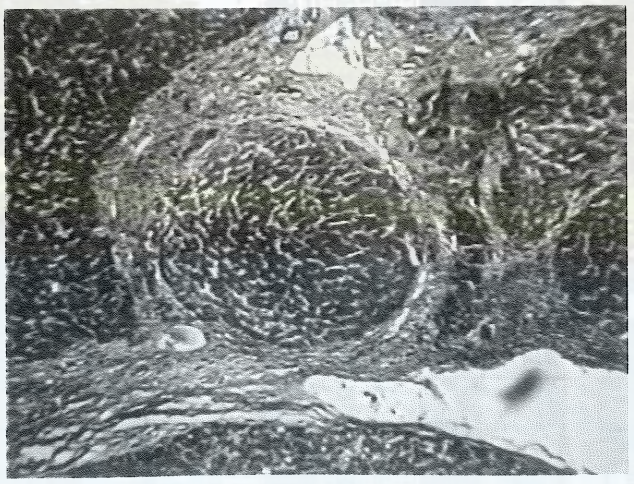
+++ CT

Hepatic tissue

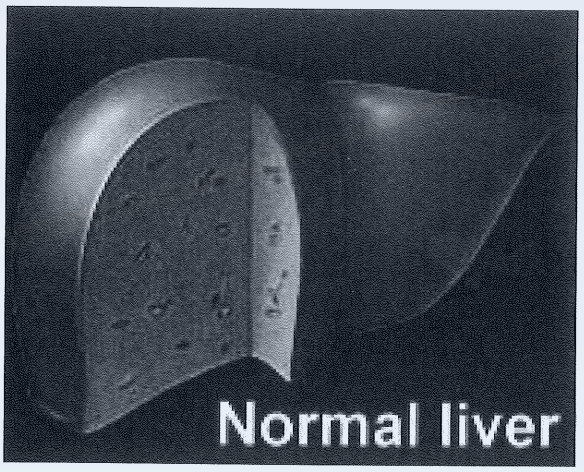


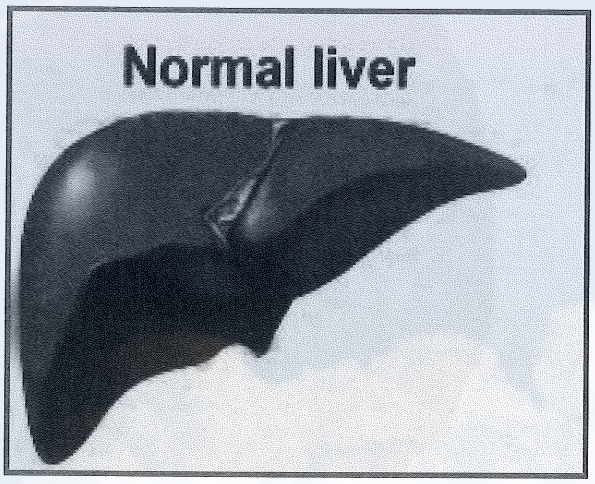
Fibrosis

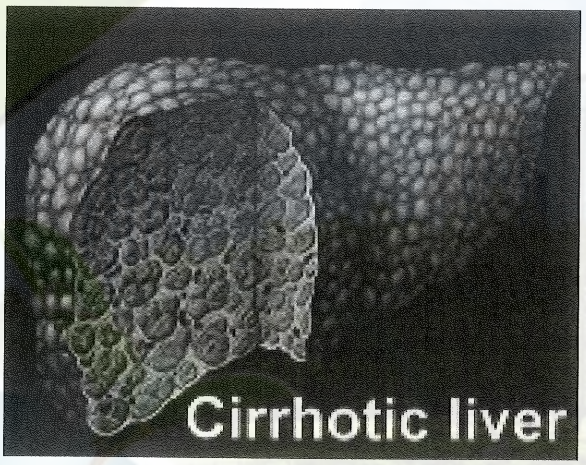
Regeneration nodules

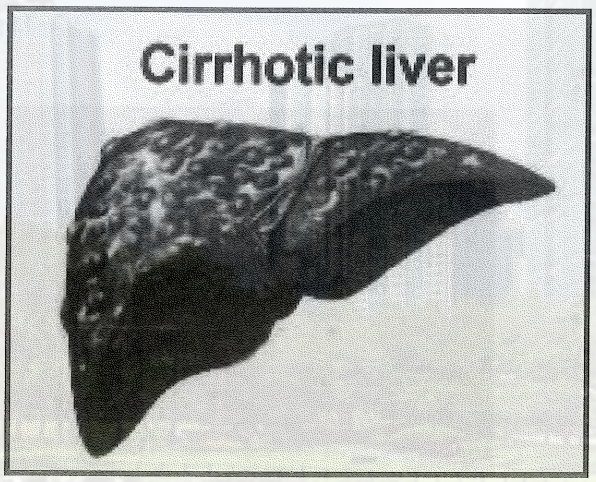


Irreversible loss of normal hepatic structure

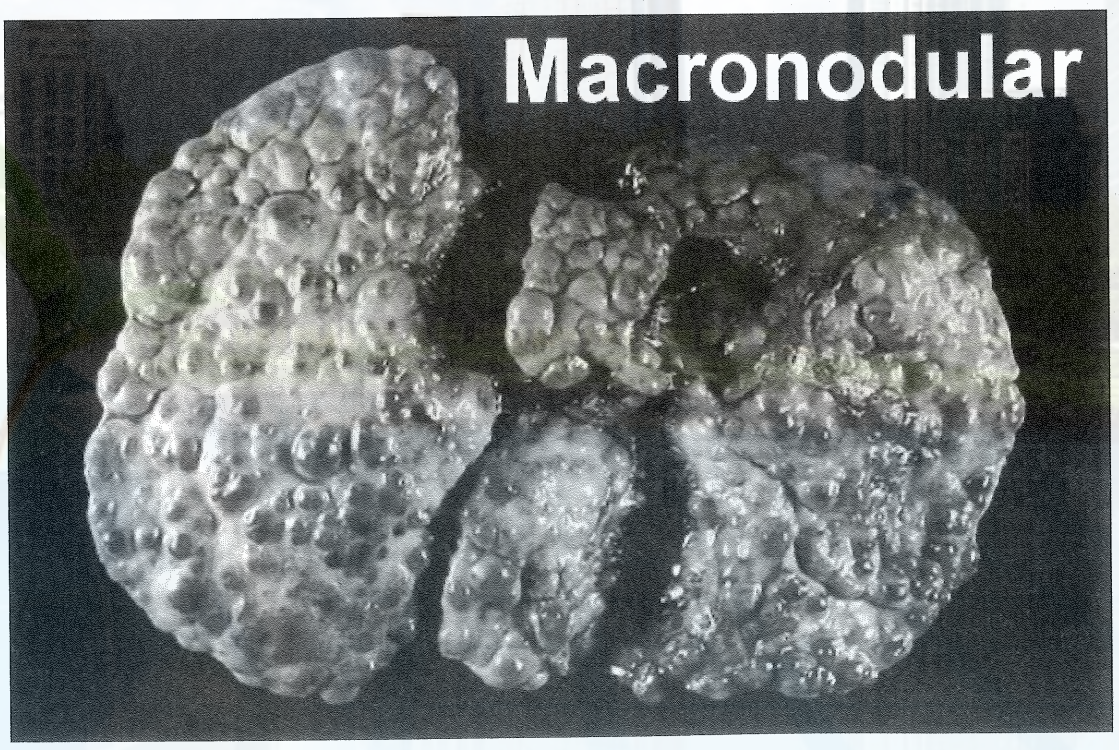

Normal liver


Normal liver


Cirrhotic liver


Cirrhotic liver

CIRRHOSIS



ETIOLOGY

A B C D

1. **A**lcoholic cirrhosis.
2. **B**iliary cirrhosis.
3. **C**ryptogenic (Idiopathic) cirrhosis.
4. **C**ardiac cirrhosis.
5. **C**hronic hepatitis: POST – HEPATITIS CIRRHOSIS
   - Postviral hepatitis *(Virus: B, C, D).*
   - Autoimmune *(Lupoid hepatitis, Primary sclerosing cholangitis).*
6. **D**rug – induced cirrhosis:
   - Alpha methyl dopa.
   - Amiodarone.
   - INH.
   - Methotrexate.
7. **MISCELLANOUS:**
   - Metabolic causes.
   - NASH.

Hepatic schistosomiasis

- There is ONLY fibrosis.
- There is No true cirrhosis: *No degeneration, No regeneration nodules, No loss of structure.*

CLINICAL PICTURE

A. Compensated " Latent " cirrhosis: [EARLY]

- ASYMPTOMATIC: **Early,** there is no impairment of liver functions.
- ACCIDENTAL DISCOVERY: of an enlarged liver & maybe an enlarged spleen:
  - During routine check up, OR:
  - During examination for a non-related condition.

B. Decompensated " Manifest " cirrhosis: [LATE]

I. *General features of cirrhosis:*

1. ABDOMINAL EXAMINATION:
   - Liver: **S**hrunken, **S**harp edge, Firm consistency.
   - Spleen: Enlarged.
2. FEATURES OF COMPLICATIONS:
   - Liver cell failure.
   - Portal HTN.
   - HCC.

II. *Specific features of cirrhosis:*

- Features according to the specific cause of cirrhosis: " see later ".

INVESTIGATIONS

I. *General investigations of cirrhosis:*

1. ABDOMINAL INVESTIGATIONS:
   - Liver imaging: Abdominal ultrasonography & CT scan.
   - LIVER BIOPSY.
2. FEATURES OF COMPLICATIONS:
   - Liver function tests: for Liver cell failure.
   - Investigations: for Portal HTN.
   - Alpha feto protein: for early detection of HCC.

II. *Specific investigations of cirrhosis:*

- For detection of the specific cause of cirrhosis: " see later ".

CHILD'S CLASSIFICATION

- The severity of liver cirrhosis can be assessed using CHILD'S CLASSIFICATION:

Class	A	B	C
Encephalopathy	None	Minimal	Advanced coma
Ascites	None	Easily controlled	Poorly controlled
Serum albumin (gm / dl)	Over 3.5	3 – 3.5	Below 3
Serum bilirubin (mg / dl)	Below 2	2 – 3	Over 3
INR	Below 1.7	1.7 – 2.3	Over 2.3

TREATMENT

I. General TTT of cirrhosis:

1. TTT of: Liver cell failure.
2. TTT of: Portal HTN.
3. TTT of: HCC.

} **Complications**

4. Antifibrotic drugs: (e.g. Colchicine, Corticosteroids) are of doubtful value.
5. LIVER TRANSPLANTATION: the only curative ttt.

II. Specific TTT of cirrhosis:

- TTT of the specific cause of cirrhosis: " see later ".

ALCOHOLIC CIRRHOSIS

ETIOLOGY

- Prolonged consumption of alcohol → toxicity to the liver cells.

PATHOLOGY

- General features of cirrhosis (usually Micronodular type).
- Liver cells may show:
  - Eosinophilic inclusions (MALLORY BODIES)
  - Fatty changes (STEATOSIS)

} **Non Pathognonmonic**

CLINICAL PICTURE

1. General picture of cirrhosis.
2. History of prolonged alcohol intake.
3. Associated complications of: **Alcoholism.**

Complications of Alcoholism

1. Cardiac:

- Coronary ***atherosclerosis***.
- Dilated cardio***myopathy***.

2. Neurological:

- Cerebral ***atherosclerosis***.
- ***Myopathy***.
- PN.
- Ataxia.
- Headache & migraine.
- Wernick's encephalopathy.
- Coma.
- Epilepsy.

3. Liver & GIT:

- Liver: *Fatty liver, hepatitis, cirrhosis.*
- GIT: *Gastritis, peptic ulcer, malabsorption, pancreatitis.*

4. BLOOD:

- Macrocytic anemia.

5. GENERAL:

- Metabolic: *↑ lipids, ↑ uric acid, ↓ magnesium, Ketoacidosis.*
- Parotid: *Bilateral parotid enlargement.*
- Palmar fascia: *Dupuytren's contracture.*

INVESTIGATIONS

1. General investigations for cirrhosis.
2. GGT: Elevated.

TREATMENT

1. General ttt of cirrhosis.
2. Stop alcohol intake.

POST – HEPATITIS CIRRHOSIS

ETIOLOGY

- It follows ***chronic hepatitis*** due to:
  - Postviral hepatitis *(Virus: B, C, D).*
  - Autoimmune *(Lupoid hepatitis).*

PATHOLOGY

1. General features of cirrhosis.
2. Features of chronic hepatitis may be present.
3. Specific pathology of the cause: e.g.
   - HBV: GGA & Positive orcein stain.
   - HCV: Lymphocyte deposits & Fatty changes (STEATOSIS).

CLINICAL PICTURE

1. General features of cirrhosis.
2. Specific past history of the cause: e.g. *Viral hepatitis*.

INVESTIGATIONS

1. General investigations of cirrhosis.
2. Specific investigations of the cause:
   - Postviral hepatitis *(Virus: B, C, D):* HEPATITIS MARKERS.
   - Autoimmune *(Lupoid hepatitis):* AUTO – ANTIBODIES.

TREATMENT

1. General ttt of cirrhosis.
2. Specific ttt of the cause: VH & Lupoid hepatitis (see later).

BILIARY CIRRHOSIS

ETIOLOGY

- It is due to: [Long standing biliary obstruction = Cholesta

  - Primary Biliary Cirrhosis (PBC) = Intra-hepatic biliary obstruction.
  - Secondary Biliary Cirrhosis = Intra or extra-hepatic biliary obstruc

I. PRIMARY BILIARY CIRRHOSIS

ETIOLOGY

- Unknown: *probably autoimmune*

- It is associated with other autoimmune diseases, e.g. *SLE, Sjogren's syndom*
- Presence of anti**M**itochondrial antibodies in the serum, High serum Ig**M**.

PATHOLOGY

1. General features of cirrhosis.
2. Specific feature of PBC: " **Injury of the interlobular or septal bile duc**

CLINICAL PICTURE

1. INCIDENCE: 90 % of the patients are females, 40 – 60 years.
2. Pruritus: is the earliest symptom.
3. Jaundice: obstructive jaundice occurs months to years after pruritus.
4. STEATORRHEA & MALABSORPTION of fat – soluble vitamins:
   - **B**one affection: osteoporosis & osteomalacia (*Hepatic osteodystr*
   - **B**leeding tendency.
5. Hepatomegaly: *enlarged, firm, with sharp edge.*
6. Splenomegaly.
7. Skin hyperpigmentation & clubbing.
8. Associated autoimmune diseases may be present, e.g. *SLE, Sjogren's syndr*

INVESTIGATIONS

1. **Liver function tests:** [Obstructive jaundice], e.g.
   - Serum alkaline phosphatase & GGT: elevated.
   - Serum bilirubin (direct): elevated.
2. **Serology:**
   - Positive Anti**M**itochondrial antibodies: *in more than 95 % of the patients*.
   - High serum Ig**M** level.
3. **Imaging:** [Abdominal ultrasonography or CT]
   - Enlarged liver with: No dilated intra-hepatic biliary radicles.
4. **Liver biopsy:**
   - Injury of the interlobular or septal bile ducts.

TREATMENT

I. General TTT of cirrhosis: (see before)
- LIVER TRANSPLANTATION: the only curative ttt.

II. Specific TTT (Symptomatic):
- Cholestyramine: *Bile salt sequestrant* (↓ pruritus).
- Ursodeoxycholic acid *↑ bile flow through the liver* (↓ cholestasis).
- FAT – SOLUBLE VITAMINS (Parentrally).

II. SECONDARY BILIARY CIRRHOSIS

ETIOLOGY

1. **Extra-hepatic biliary obstruction:** *Extra-hepatic cholestasis*
   - Obstruction: in LARGE bile ducts that lie OUTSIDE the liver (***CBD or its main branches***).
   - Causes: see obstructive jaundice.
2. **Intra-hepatic biliary obstruction:** *Intra-hepatic cholestasis*
   - Obstruction: in SMALL bile ducts that lie WITHIN the liver.
   - Causes: see obstructive jaundice.

CLINICAL PICTURE

1. Features of obstructive jaundice: *of long duration*.
2. Features of the cause of obstructive jaundice.
3. General features of cirrhosis: *following longstanding obstructive jaund*

INVESTIGATIONS

1. Liver function tests: [Obstructive jaundice], e.g.

- Serum alkaline phosphatase & GGT: elevated.
- Serum bilirubin (direct): elevated.

2. Investigations for the cause of obstructive jaundice:

- **Imaging** [Abdominal ultrasonography or CT]

1. **Extra-hepatic biliary obstruction:** *Extra-hepatic cholest*
   - Enlarged liver with: dilated intra-hepatic biliary radicles.

2. **Intra-hepatic biliary obstruction:** *Intra-hepatic cholest*
   - Enlarged liver with: No dilated intra-hepatic biliary radi

3. General investigations of cirrhosis.

TREATMENT

I. General TTT of cirrhosis: (see before)

II. Symptomatic TTT:

- Cholestyramine: *Bile salt sequestrant* (↓ pruritus).
- Ursodeoxycholic acid *↑ bile flow through the liver* (↓ cholestasis).
- FAT – SOLUBLE VITAMINS (Parentrally).

III. Specific TTT of the cause: e.g.

- Surgical removal of gall stones.

CARDIAC CIRRHOSIS

ETIOLOGY

"Congestive Hepatopathy"

- It is due to: [Long standing hepatic venous congestion]
  1. Prolonged severe RVF.
  2. Tricuspid valve disease: *(TS, TR).*
  3. Prolonged severe pericardial disease *(pericardial effusion, CP).*
  4. High IVC obstruction.
  5. Budd-Chiari syndrome.
  6. Veno-occlusive disease *(VOD).*
- Long standing hepatic venous congestion will lead to:
  1. ↓ drainage of sinusoidal blood flow into terminal hepatic venules → sinusoidal stasis.
  2. Sinusoidal stasis → accumulation of deoxygenated blood, parenchymal atrophy, necrosis, collagen deposition, and, ultimately, fibrosis.

PATHOLOGY

1. General features of cirrhosis.
2. Centrilobular congestion.

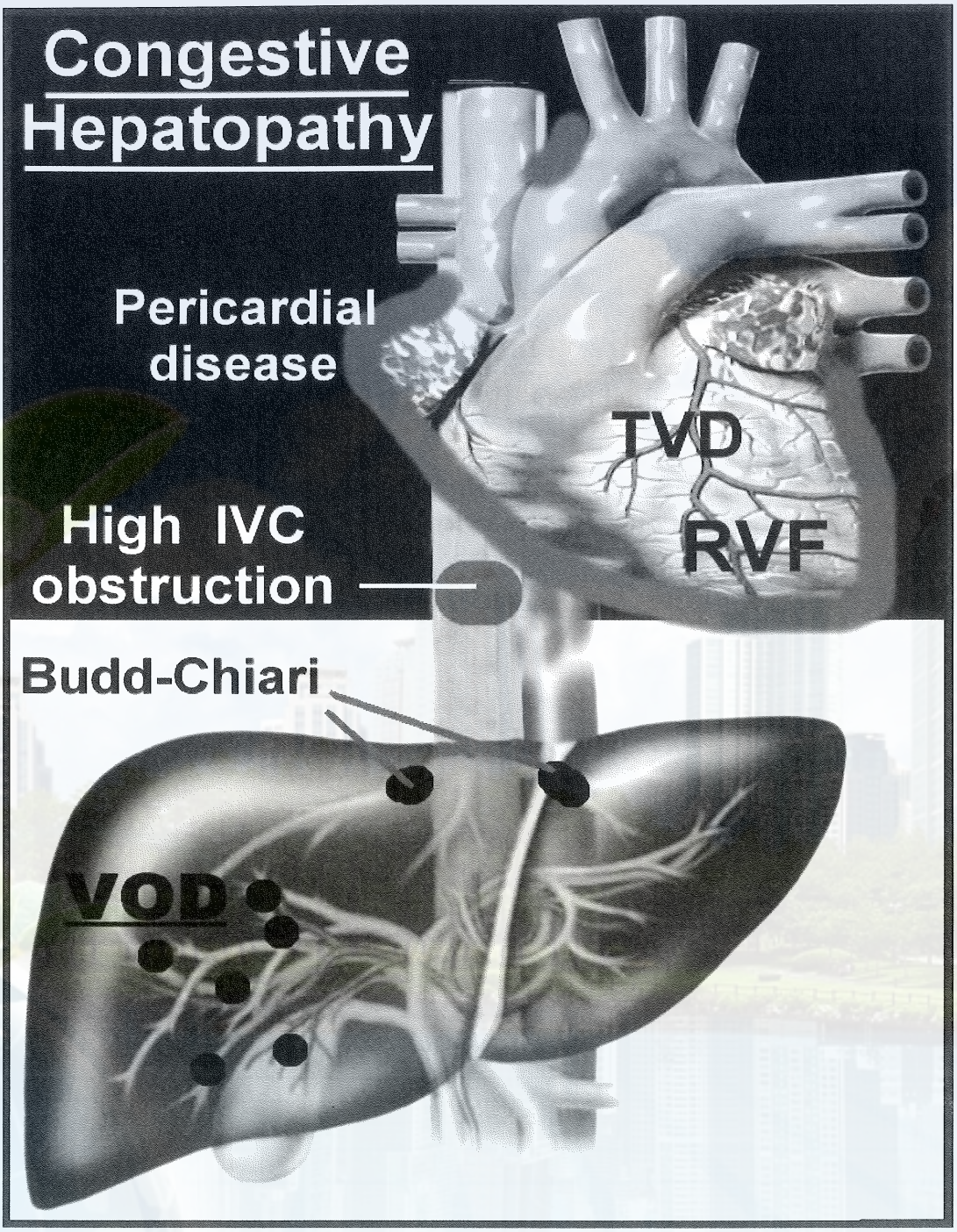
CLINICAL PICTURE

1. General features of cirrhosis.
2. Liver: enlarged, firm, TENDER, with sharp edge.
3. Specific features of the cause, e.g. RVF.

INVESTIGATIONS

1. General investigations of cirrhosis.
2. Liver imaging: [Abdominal ultrasonography & CT scan]
   - *Enlarged congested liver.*
   - *Prominent hepatic veins.*
3. Specific investigations of the cause, e.g. cardiac imaging (echocardiography).

CARDIAC CIRRHOSIS



TREATMENT

1. General ttt of cirrhosis.
2. Specific ttt of the cause, e.g. RVF.

BUDD-CHIARI SYNDROME

- Obstruction of the **LARGE** hepatic veins due to:
  1. Thrombosis: Hypercoagulation (e.g. *PRV, PNH, CCPs),* Behcet's syndrome.
  2. Invasion from outside: Malignancy.
  3. No cause: In many cases (~ 30 %).

- CLINICAL PRESENTATIONS:
  1. Acute:
     - *Acute abdominal **pain**, **hepatomegaly**, **ascites** & mild jaundice.*
     - *Acute liver failure may occur.*
  2. Chronic:
     - *Features of cardiac cirrhosis.*

- INVESTIGATIONS:
  1. General investigations of cirrhosis.
  2. Specific investigations for Budd – Chiari syndrome: **[IMAGING]**
     - *MRV.*
     - *Duplex ultrasound.*

- TREATMENT:
  1. General ttt of cirrhosis.
  2. Specific ttt of Budd – Chiari syndrome:
     - *Acute: Fibrinolytic therapy, followed by anticoagulants.*
     - *Chronic: Anticoagulants, to prevent further thrombosis.*

VENO-OCCLUSIVE DISEASE

- Obstruction of the **SMALL & MEDIUM-SIZED** hepatic veins due to
  1. Toxic injury by a toxin: Senecio alkaloid present in a special type of *medicinal t*
  2. Chemotherapy, Radiotherapy.
  3. Following BMT (using cyclophospamide).

- CLINICAL PRESENTATIONS: *"A disease of CHILDREN"*
  - The same as Budd – Chiari syndrome.

- INVESTIGATIONS:
  - The same as Budd – Chiari syndrome.

- TREATMENT:
  - The same as Budd – Chiari syndrome.

METABOLIC CIRRHOSIS

ETIOLOGY

1. Hemochromatosis " Iron overload ".
2. Wilson's disease " Copper overload ".
3. Alpha 1- antitrypsin deficiency.

1. HEMOCHROMATOSIS " Bronze Diabetes "

DEFINITION

- Iron storage disorder: Massive generalized iron deposits in various organs.
- Tissue damage: Functional impairment in various organs.

ETIOLOGY

1. PRIMARY: " HEREDITARY "
   - Unknown defect: [Excessive intestinal iron absorption].
2. SECONDARY:
   a) Increased production: chronic hemolytic anemia especially *Thalassemia*.
   b) Decreased utilization: sideroblastic anemia.
   c) Increased intake:
      - ↑ parentral intake: *repeated iron injections* & *repeated blood transfusions*.
      - ↑ dietary intake: *medicinal tonics* & *red wine*.

CLINICAL PICTURE "S H I P"

- **S**ex: usually ***males*** between 40 – 60 years.
- **S**kin: ***hyperpigmentation*** (bronze coloration).
- **S**uprarenal: adrenal insufficiency.

- **H**epatic: ***liver cirrhosis*** → ***HCC*** (25 %).
- **H**eart: ***cardiomyopathy***.

- **I**nfections: uncommon.

- **P**ituitary: ***hypogonadism*** (testicular atrophy, impotence, ↓ libido, ster
- **P**arathyroid: ***hypoparathyroidism***.
- **P**ancreas: secondary ***diabetes***.
- **P**olyarthritis.

- OTHERS: mental disturbances.

INVESTIGATIONS

1. General investigations for cirrhosis.

2. Investigations suggesting IRON OVERLOAD:

a) *Laboratory:*

- Serum iron, ferritin, transferrin saturation: increased.
- TIBC: decreased.

b) *Liver Imaging:* *" Abdominal CT & MRI "*

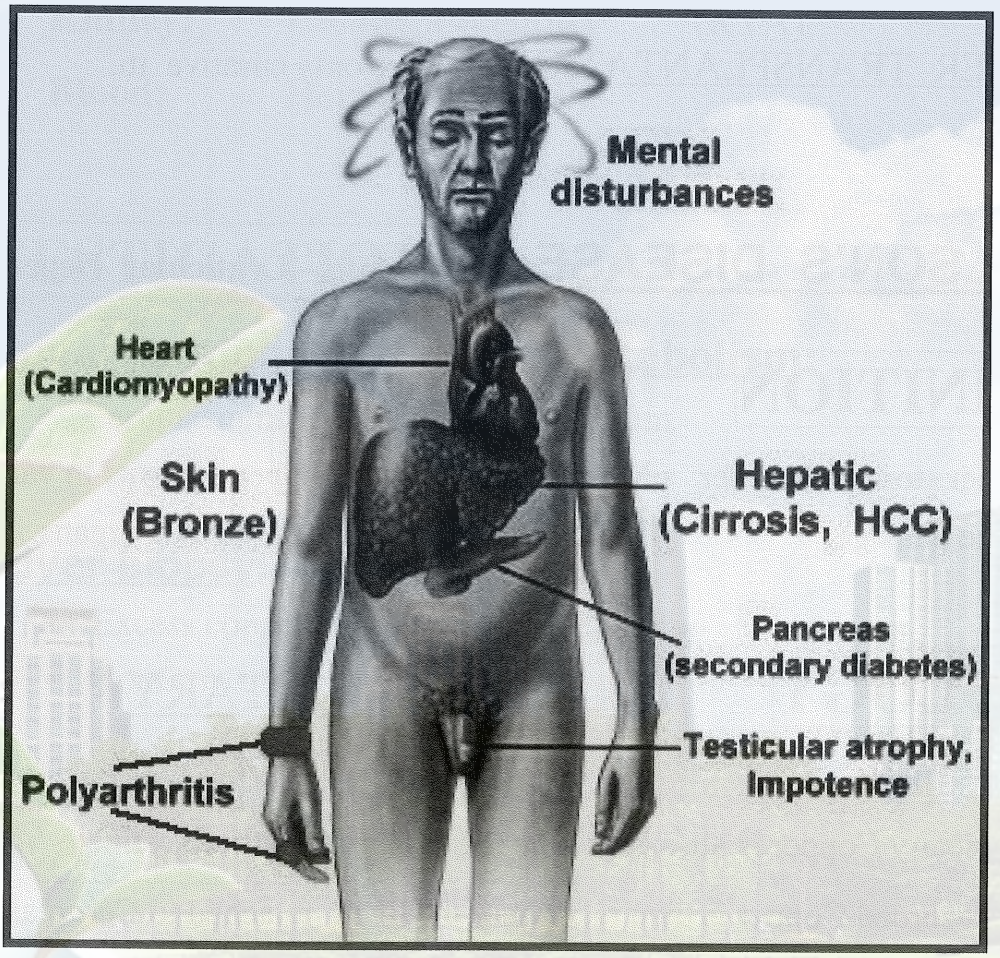
- Excess iron deposition in the liver.

c) *Liver biopsy:*

- Excess iron deposition in the liver.
- Confirms cirrhosis.

HEMOCHROMATOSIS " Bronze Diabetes "

"Iron is essential for the body ……., but:
Too much iron is dangerous ….."



TREATMENT

1. Restriction of iron in diet.
2. Removal of excess iron:
   - Iron chelation: *DESFERRIOXAMINE* ↑ urinary excretion of i
   - Repeated venesection.
3. Symptomatic treatment: e.g. DM, HF.
4. LIVER TRANSPLANTATION: the only curative ttt.

2. WILSON'S DISEASE "Hepato – Lenticular Degeneratio

DEFINITION

- Copper storage disorder: Massive generalized copper deposits in various or
- Tissue damage: Functional impairment in various organs.

ETIOLOGY "HEREDITARY"

- Normally:
  - Dietary Copper is absorbed from the proximal small intestine.
  - Absorbed Copper is then taken into the liver, attached to Ceruplasmin and released to the blood.
  - Copper is excreted from the body through the BILE.
- In Wilson's disease:
  - Mutation → decreased excretion of Copper through the bile → → Copper builds up in the liver and injures liver tissue.
  - Deficiency of Ceruplasmin → Free Copper will be released to the blood Excess Copper will build up in blood & will be deposited in the tissues.

CLINICAL PICTURE

- **Liver:** Cirrhosis, Hepatitis *(chronic or acute).*
- **Brain:**
  - *Extrapyramidal disease (Parkinsonism or chorea).*
  - *Mental disturbances (Dementia).*
- **Eye:** Kayser-Fleischer rings (greenish-brown rings).
- **Kidney:** Tubular affection (RTA).
- **Blood:** Hemolytic anemia.

INVESTIGATIONS

1. Investigations of Copper metabolism:

- Ceruplasmin: decreased in serum.
- Copper: decreased in serum & increased in urine.

2. Liver biopsy:

- Excess copper deposition in the liver.
- Confirms cirrhosis.

TREATMENT

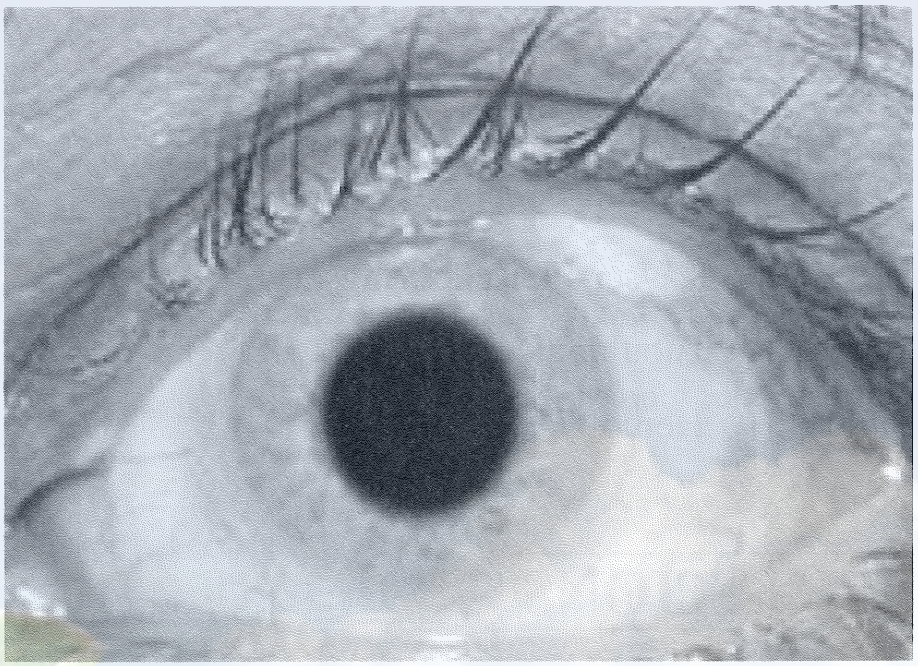
1. Restriction of copper in diet.

2. Removal of excess copper:
   - Copper chelation: *PENICILLAMINE* ↑ urinary excretion of copper.
   - K sulphide: precipitates copper in the intestine.

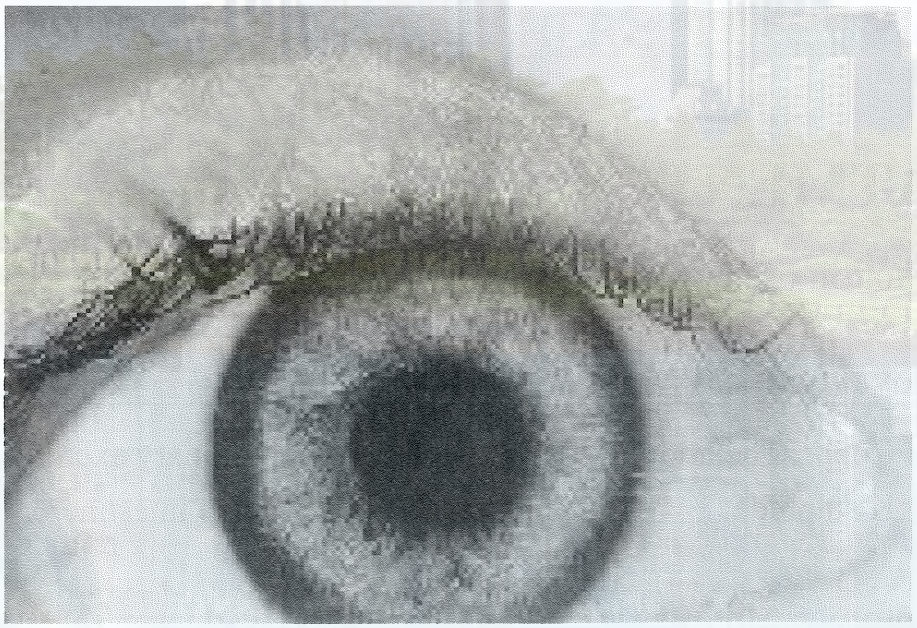
3. Symptomatic treatment: e.g. Parkinsonism.

4. LIVER TRANSPLANTATION: the only curative ttt.

Normal eye



Kayser-Fleischer ring



3. ALPHA 1- ANTITRYPSIN DEFICIENCY

- A genetic disorder which presents with:
  - Liver: liver cirrhosis, chronic hepatitis.
  - Lung: emphysema (primary).

LIVER CELL FAILURE

ETIOLOGY

1. **Advanced** cases of:
    - Liver cirrhosis.
    - Chronic active hepatitis.
    - Obstructive jaundice.
    - Hepatic malignancy.
2. **I**nfections:
    - Viral hepatitis: *B, C, D.*
    - Other viruses causing hepatitis: *EBV, CMV, HSV, Yellow fever.*
3. **I**atrogenic & (Toxins):
    - Alcohol.
    - Halothane.
    - INH, Methotrexate.
    - Carbon tetrachloride, DDT, Phosphorus.

CLINICAL MANIFESTATIONS

1. Failure of health.
2. Fever & septicemia.
3. Fetor hepaticus.
4. Jaundice.
5. Cardiovascular manifestations
6. Ascites.
7. Skin manifestations.
8. Hepato-renal syndrome.
9. Hepatic encephalopathy
10. Hematological manifestations.
11. Endocrinal manifestations
12. Disturbed carbohydrate metabolism.
13. Increased incidence of infections.

CLINICAL MANIFESTATIONS

FAILURE OF HEALTH

- Weakness, Weight loss.

FEVER & SEPTICEMIA

- ***Low grade fever:***

  PYROGENS released due to necrosis of the liver cells.

- ***Septicemia:***

  Failure of the liver to clear bacteria from the circulation, or:
  Bacteria bypass the liver through porto – systemic shunts.

FETOR HEPATICUS

- ***Sweetish, fecal smell:***

  Failure of detoxification of mercaptans absorbed from the intestine due to:
  liver failure or *shunts*.

JAUNDICE

- ***Hepatocellular jaundice:***

  Failure of the liver cells to metabolize bilirubin.

CARDIOVASCULAR MANIFESTATIONS

1. Hyperkinetic circulation:
   - Overproduction & decreased destruction of: *vasodilator materials*.
2. Central cyanosis & clubbing:
   - Pulmonary AV shunts: *due to vasodilator materials*.
   - Porto-pulmonary shunts.
   - Basal lung collapse due to tense ascites.

ASCITES

- ***Incidence:***

It is common in liver failure secondary to liver cirrhosis.

- ***Onset:***

1) Gradual: the usual presentation in liver cirrhosis (common).

2) Acute: ascites may develop rapidly if the liver function is ↓↓ acutely:

- Shock.
- Hemorrhage.
- Infection.
- Portal vein thrombosis.

- ***Course:***

It may be followed by: oedema LLs, plerural effusion, pericardial effusion

- ***Pathogenesis:*** " Pathogenesis of ascites in liver cirrhosis "

1. Hypoalbuminemia: Due to diminished synthesis of **albumin** by the liver.
" The ascitic threshold " for albumin is: 3 gm %.

2. Portal Hypertension: It rarely produces ascites.
It localizes the transudate to the peritoneal cavity.

3. Salt & water retention: "Through stimulation of the **RAAS**"

- ***Overflow Theory:*** salt retention is ***primary*** & then it starts the development of ascite
- ***Underfill Theory:*** salt retention is ***secondary*** to ascites & then it aggravates ascites

4. Lymphorrhea: In post-sinusoidal obstruction, there is dilatation of the lymphatics on the surface of the liver with extravasation of lymph into the peritoneal cavity

5. Complications: Development of *TB peritonitis, malignancy or SBP*

Most recent theory **"The peripheral arterial VD theory"**

- Cirrhosis → arterial VD → ↓ splanchnic & systemic vascular resistance →
→ pooling of blood in the splanchnic circulation → ↓ effective AB volume →
→ stimulation of the **RAAS** → salt retention → ascites.

SKIN MANIFESTATIONS

1. **Arterial spiders "Spider naevi":** ***due to estrogen excess***
   - They consist of a central dilated arteriole with radiating capillaries.
   - Compression of the central arteriole, causes blanching of the whole lesion.
   - They are found in the distribution of the SVC (face, neck, UL & upper chest).

2. **Palmar erythema:** ***due to estrogen excess***
   - The hands are warm.
   - The palms are bright red in colour, especially the thenar & hypothenar eminences, and the heads of the metacarpal bones.

3. **Paper-money skin:** ***due to estrogen excess***
   - Numerous small vessels scattered through the skin in random fashion.

4. **White nails:** ***due to hypoproteinemia***
   - Opacity of the nail bed with a pink zone at the tip of the nail.

Causes of PALMAR ERYTHEMA

P Polycythemia, Pregnancy.

A Alcohol intake, Autoimmune (RA, SLE).

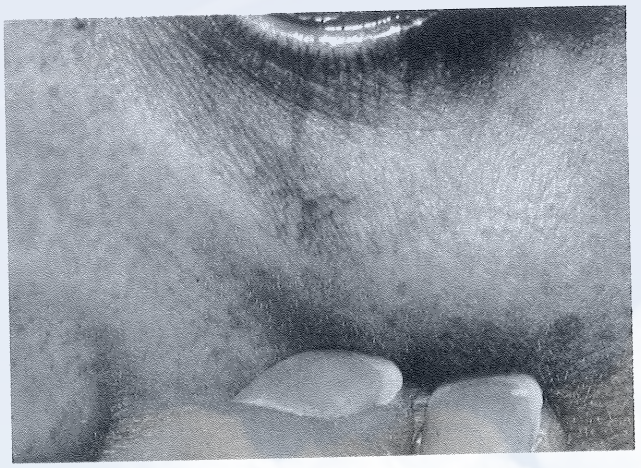
L Liver cell failure, Leukemia.

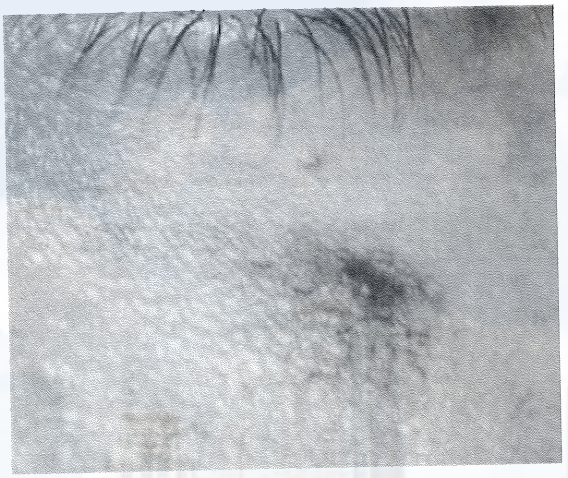
M Medications (CCPs, Corticosteroids), Miscellaneous (Thyrotoxicosis).

HEPATO-RENAL SYNDROME

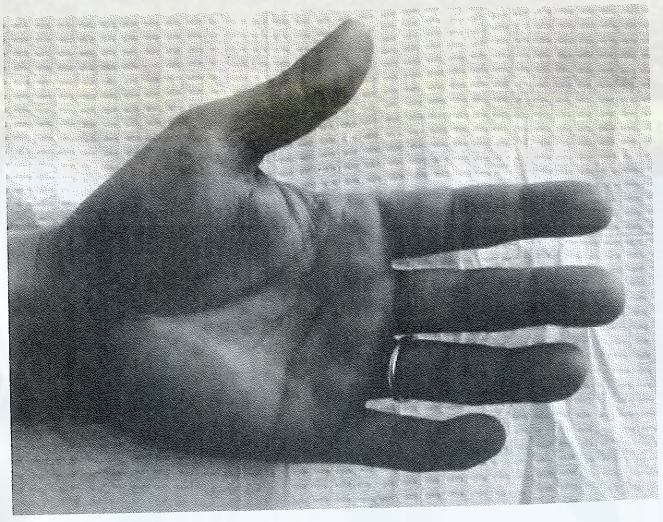
- Renal failure with NORMAL renal histology occurring in patients with severe liver disease.
- *Etiology:*
  - Decreased effective plasma flow due to: systemic VD, ascites, diuretics.
  - VC of the afferent renal arterioles due to: ↑ Vasopressin.
- *Precipitating factors:* excessive diuresis, diarrhea, vomiting, infection, tapping of ascites.
- *Prognosis:* it carries a very bad prognosis & is usually fatal.
- *Treatment:* avoid: the precipitating factors.
  give: IV albumin (plasma expander), **plus,**
  Octreotide (causes systemic VC).

Spider naevi





Palmar erythema



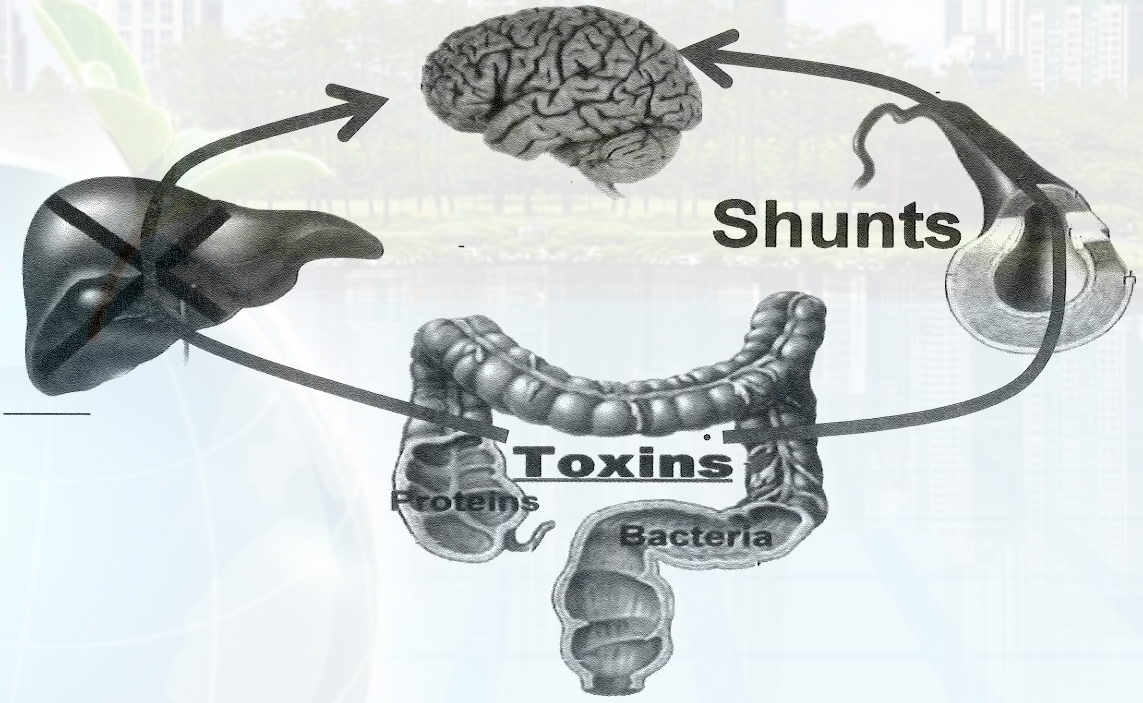
HEPATIC ENCEPHALOPATHY

- It is a **neuropsychiatric syndrome** that may complicate severe liver disease.

- **Pathogenesis:**

1. Production of toxic substances: *by the action of BACTERIA on intestinal proteins*
   - These toxic substances will either pass through the diseased liver without detoxification or will bypass the liver through the porto-systemic shunts.
   - These toxic substances will then reach the CNS & lead to encephalopathy because they will disturb the cerebral metabolism.
   - *These toxic substances include:*
     - Ammonia: It interferes with Kreb's cycle → ↓ energy supply to brain.
     - Amines: Mercaptans, Serotonin.
2. Disturbance of amino acids:
   a) *Increased aromatic aa & decreased branched aa will result in:*
     - Decreased production of normal neurotransmitters (as noradrenaline).
     - Increased production of false neurotransmitters (as octapamine).

   b) *Increased level of GABA which is an inhibitory neurotransmitter.*
3. Alkalosis & Hypokalemia:
     - They increase the renal production of ammonia.
     - They facilitate the passage of toxic substances through the BBB.



- **Important question:** **"Self – assessment"**

"Give reasons for: *Alkalosis* & *Hypokalemia* in liver cell failure".

PRECIPITATING FACTORS "4 M"

1. Much NITROGEN load:

- Excess dietary protein.
- Constipation.
- Azotemia.
- GIT bleeding (e.g. Hematemesis):
  - *It ↑ intestinal toxins due to action of bacteria on blood proteins.*
  - *It ↓ the hepatic blood flow & thus worsens liver functions.*
  - *It ↓ the renal blood flow & thus worsens renal functions.*

2. METABOLIC disturbances:

- Alkalosis.
- Hypokalemia.
- Hyponatremia.
- Hypovolemia.

3. MEDICATIONS:

- Narcotics *(e.g. Morphine)*, Sedatives, *(e.g. Benzodiazepines)*.
- Diuretics *(e.g. Frusemide)*.

4. MISCELLANEOUS:

- **S**BP, and *INFECTIONS* in general.
- **S**urgery: e.g. for *portal hypertension*.
- **S**evere vomiting or diarrhea.
- **T**ransfusion of stored blood.
- **T**apping of ascites.
- **T**IPS.

- Clinical Picture: *2 stages*

1. Precoma: **S A D**

- **S**leep disturbances: somnolence & inverted sleep rhythm.
- **S**peech disturbances: slurred speech or monotonus speech.
- **A**pathy.
- **A**sterixis.
- **D**isturbed personality & behaviour: childish attitude & irritability.
- **D**CL with disorientation for: *time, place, persons.*

2. Coma:

- Irritable coma with features of liver failure & finally death.

- Classifications & Grading:

- Recently, hepatic encephalopathy has been classified according to severity into:

"West Haven Criteria"

GRADE	*MENTAL STATUS*	*NEUROLOGICAL FINDINGS*
Grade 1	Mild disorientation Inverted sleep rhythm	Astrexis may be detected
Grade 2	Lethargy *or* apathy Inappropriate behavior	Astrexis obvious
Grade 3	Marked disorientation Somnolence	Astrexis obvious
Grade 4	**COMA**	**COMA**

- Also, in the World Congress of Gastroenterology 1998 in Vienna, hepatic encephalopathy was subdivided into 3 subclasses, Type A, B and C:
  - Type **A** (= **A**cute): associated with **A**cute liver failure.
  - Type **B** (= **B**ypass): is caused by porto – systemic shunting (**B**ypass) without associated intrinsic liver disease.
  - Type **C** (= **C**irrhosis): occurs in patients with **C**irrhosis.

HEMATOLOGICAL MANIFESTATIONS A B C

A. Anemia:

1. Microcytic hypochromic anemia: due to repeated hemorrhages, **e.g.** *oesophageal va*
2. Normocytic normochromic anemia: due to acute hemorrhage or hypersplenism.
3. Macrocytic anemia: due to deficiency of folic acid or vitamin B12.

B. Bleeding tendency:

I. Defect in the clotting factors "Deficiency", especially:

- PROTHROMBIN
- Fibrinogen.
- Factors V, VII, IX, X.

II. Defect in the platelets:

1. Thrombocytopenia: " Decreased platelets ": due to hypersplenis
2. Thrombocytopathy: " Diseased platelets ".

C. Cytopenia:

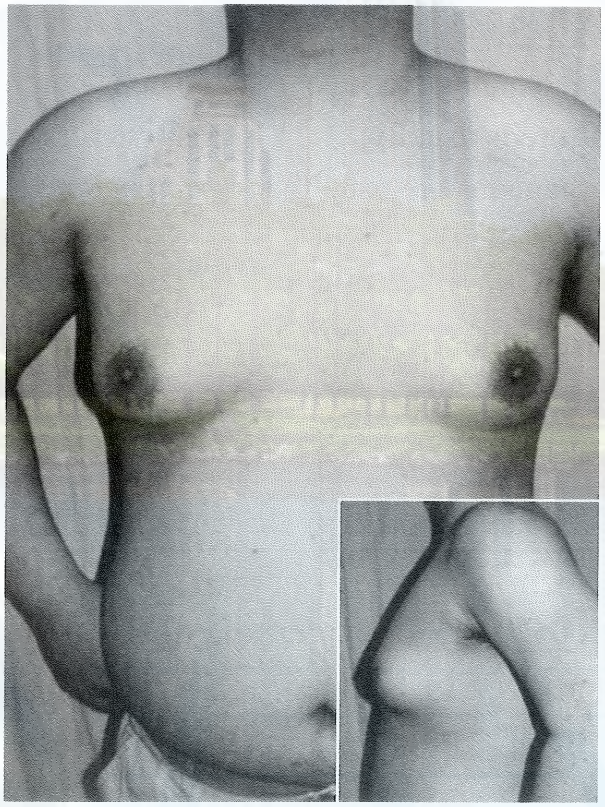
Pancytopenia due to hypersplenism.

ENDOCRINAL MANIFESTATIONS

1. In males: [*Feminization*]
   - Gynecomastia.
   - Testicular atrophy, impotence, ↓ libido, sterility.
   - Feminine distribution of suprapubic hair.
2. In females: [*Defeminization*]
   - Atrophy of the breasts.
   - Amenorrhea, ↓ libido, sterility.

- The mechanism of these endocrinal manifestations is unclear, but may be du
  - Increased estrogen.
  - Decreased testosterone.
  - Increased sex hormone-binding globulin (SHBG).

Gynecomastia



DISTURBED CARBOHYDRATE METABOLISM

- In chronic liver failure: IGT & rarely secondary diabetes.
- In acute liver failure: Hypoglycemia.

INCREASED INCIDENCE OF INFECTIONS

Spontaneous Bacterial Peritonitis " SBP "

Definition

- Infected ascitic fluid with no clear cause for peritonitis.
- It is probably due to ↓ antibacterial activity of the ascitic fluid in cirrhosis.

Clinical picture

- It occurs in about 10 % of cirrhotic patients with ascites.
- Sudden deterioration of a cirrhotic patient & encephalopathy with no obvious ppt. factor.
- *Fever, abdominal pain, tenderness, REFRACTORY ASCITES.*

Ascitic fluid analysis

- Polymorph count usually exceeds: 250 cells / cmm.
- Ascitic fluid culture is usually: positive for organisms.
- The infecting organisms are usually: *gram negative organisms*.

Treatment

- Broad spectrum antibiotics: Cephalosporins, Ciprofloxacin.

INVESTIGATIONS

1. Liver function tests:

- Plasma proteins: ↓ albumin, ↑ globulin, reversed A/ G ratio.
- Prothrombin time: Prolonged, & not corrected by parentral vitamin K
- Serum bilirubin: ↑ both direct & indirect.
- Serum enzymes: ↑ transaminases & ↑ alkaline phosphatase.

2. Investigations for the cause:

e.g. Abdominal ultrasonography or CT scan for *cirrhosis*.
e.g. HEPATITIS MARKERS for *hepatitis*.

3. Investigations for the precipitating factors:

e.g. serum potassium.

4. Investigations to exclude other causes of coma:

in case of hepatic encephalopathy, e.g. brain imaging & lab tests.

TREATMENT

1. **TTT of the cause:** *if possible.*
2. **TTT of the precipitating factors:** *if present.*
3. **TTT of ascites:** *if liver failure is minimal & no encephalopathy.*
4. **TTT of bleeding tendency:** *FFP to replace coagulation factors.*
5. **TTT of hepatic encephalopathy:** **Care of the comatosed**

A) DIET:

- Protein restriction: 1 gm / Kg / day.
- Carbohydrate excess: to decrease protein catabolism.
- Potassium excess: fruit juices.

B) BOWEL STERILIZATION:

- Neomycin: 1 gm / 6 hours to prevent action of intestinal bacteria on proteins.
- Metronidazole: 0.5 gm / 6 hours in cases of associated renal impairment.

C) COLONIC LAVAGE:

- Enemas to wash the intestinal contents & thus decrease the production of toxic substances by the effect of bacteria on proteins.

D) LACTULOSE:

- It is a ***synthetic disaccharide*** metabolized by the intestinal bacteria causing:
  1. Production of acids → ↓ fecal pH → change the bacterial flora.
  2. Laxative effect washing the intestinal contents.

E) Other measures:

- **L – ornithine L – aspartate (LoLa):** **"Hepamerz"**
  - It reduces the level of ammonia.

- **Drugs of doubtful value (Bad drugs):** **"3 B"**
  - **B**ranched aa: to correct their level.
  - **B**romocryptine & L-dopa: to improve neurotransmission.
  - **B**enzodiazepine antagonists.

- **Sedatives:**
  - They should be avoided, but if necessary, give: very *small doses* of: *diazepam*.
  - Morphine is absolutely contraindicated.

- **Artificial hepatic support:** **" charcoal hemodialysis "**
  - Charcoal filters are used to adsorb toxins from the blood of the patient.

6. HEPATIC TRANSPLANTATION:

- It is the only curative FINAL treatment for liver failure.

- **Important question:** **"Self – assessment"**

"Enumerate the general indications of Bromocryptine".

LIVER FUNCTION TESTS

TESTS FOR BILE PIGMENTS

I. Serum Bilirubin:

- *Total Bilirubin:*
  - Normally: 0.2-1 mg / dl.
  - In disease: It increases in: ALL TYPES OF JAUNDICE.

- *Type of Bilirubin:*
  - **Direct (conjugated) Bilirubin:**
    - Normally: 20 % of Total Bilirubin.
    - In disease: It increases in: OBSTRUCTIVE JAUNDICE.
  - **Indirect (unconjugated) Bilirubin:**
    - Normally: 80 % of Total Bilirubin.
    - In disease: It increases in: HEMOLYTIC JAUNDICE.
  - **Direct & Indirect (Biphasic) Bilirubin:**
    - Both types increase in: HEPATOCELLULAR JAUNDICE.

II. Bilirubin in urine:

- Normally: Bilirubin is ***absent*** in urine.
- In disease: Bilirubin is ***present*** in urine in: *Obstructive & Hepatocellular jaundice*.

III. Urobilinogen in urine:

- Normally: 0.5-2 mg / day.
- In disease: It ***increases*** in: *Hemolytic & Hepatocellular jaundice*.
  It ***decreases*** in: *Obstructive jaundice*.

IV. Stercobilinogen in stools:

- Normally: 50-200 mg / day.
- In disease: It ***increases*** in: *Hemolytic jaundice*.
  It ***decreases*** in: *Obstructive & hepatocellular jaundice*.

V. Bile salts in urine:

- Normally: ***absent*** in urine.
- In disease: ***present*** in urine in: *Obstructive & hepatocellular jaundice* .

SERUM ENZYMES

1. Transaminases:

- Serum Glutamic Oxalacetic Transaminase (SGOT) = Aspartate Transaminase (AST).
- Serum Glutamic Pyruvic Transaminase (SGPT) = Alanine Transaminase (ALT).

- Normally: AST is present in: Liver, heart, kidney, skeletal muscles.
  ALT is present in: Liver.

- In disease: These enzymes increase in DAMAGE of these organs (acute disease

- Conclusion: ALT is ***more specific*** for LIVER DISEASES than AST.

AST increases in: active liver damage, acute myocardial infarction, acute kidney affection, myopathy *(severe cases)*

ALT increases in: active liver disease, **e.g.** viral hepatitis.

2. Alkaline Phosphatase (ALP):

- Normally: It is formed mainly in: LIVER & BONE (3-13 King Armstrong uni
- In disease: It increases in:
  - **Marked increase in:**
    - LIVER DISEASE: *OJ, Space occupying lesions, Infiltrative disease of the liv*
    - BONE DISEASE.
  - **Moderate increase in:**
    - HEPATOCELLULAR DISEASES: *Hepatitis & Cirrhosis.*

How to confirm that increased ALP is due to LIVER DISEASE & not BONE DISEASE

- Associated increase in GGT.
- Associated increase in 5-nucleotidase.
- Abdominal ultrasonography.

3. Gamma Glutamyl Transpeptidase (GGT):

- It increases in: 1. Biliary obstruction. 2. Hepatocellular diseases (esp. Alcoholic hepati

4. Serum 5-nucleotidase:

- It increases in: - Biliary obstruction.

TESTS FOR PROTEINS

A. Chemical Separation of Plasma proteins:

- Total proteins: 6 – 8 gm / dl.
- Albumin: 4 – 5 gm / dl.
- Globulin: 2 – 3 gm / dl.
- A / G ratio: 2 / 1.

- CHRONIC LIVER DISEASE (e.g. liver cirrhosis):
  - Albumin: Decreases.
  - Globulin: Increases.
  - A / G ratio: Reversed.

- ACUTE LIVER DISEASE (e.g. viral hepatitis):
  - Albumin: Is not affected (because it has a long half life).
  - Globulin: Increases.

HYPOALBUMINEMIA is a marker of chronic liver disease

B. Electrophoresis of Plasma Proteins:

- **Albumin:** *synthesized in the LIVER*

  It ↓ in CHRONIC Liver disease but not in acute liver disease.

- **Alpha – 1 Globulin (e.g. Alpha – 1 antitrypsin):** *synthesized in the LIVER*

  It ↓ in CHRONIC Liver disease & in Alpha – 1 antitrypsin deficiency.

- **Alpha – 2 Globulin & ß – Globulin (e.g. LDL):**
  - They are LIPOPROTEINS that are excreted in bile.
  - They increase in Obstructive jaundice.

- **Gamma Globulins:** *synthesized in the RES*

  They increase in diseases that stimulate the RES:
  - Acute & Chronic liver diseases.
  - Autoimmune diseases.
  - Infections & malignancy.

TESTS FOR FATS

- Normally: Blood cholesterol is 150 – 200 mg %.
- In disease:
  - In Obstructive jaundice: Increased cholesterol, with normal esterificatio
  - In Liver failure: Normal cholesterol, with decreased esterificati

TESTS FOR CARBOHYDRATES

- **Glucose Tolerance Test:** ***of limited value in assessment of liver diseases***
  - In chronic liver failure: IGT & rarely secondary diabetes.
  - In acute liver failure: Hypoglycemia.

PROTHROMBIN TIME (PT)

- Normally: Prothrombin time (PT) is 12 – 14 sec.
  Prothrombin concentration (PC) is 100 %.
- In disease: PT is prolonged & PC is decreased in:
  1. Obstructive jaundice & other causes of Vitamin K deficiency:
     - Parentral Vitamin K ***will correct*** the PT & PC.
  2. Liver cell failure (acute & chronic):
     - Parentral Vitamin K ***will not correct*** the PT & PC.

CLINICAL IMPORTANCE OF PT

1. To assess the severity & prognosis of liver diseases.
2. Before any invasive technique or surgery.
3. Follow up of oral anti – coagulants.

TESTS FOR DETOXIFICATION

1. Bromosulphalein test (BSP):

- This dye is given in a dose of 5 mg / Kg IV.
- Normally: 90 % of the dye is cleared from the blood after 45 minutes.
  This needs: *normal hepatic blood flow*, *normal liver function*, *patency of the biliary system*.
- In disease: The dye will not be cleared from the blood after 45 minutes.
  This occurs in: *defective hepatic blood flow*, *abnormal liver function*, *obstruction of the biliary system*.

2. Indocyanin Green:

- It is safer & more specific than BSP.

ALPHA FETO-PROTEIN (AFP)

- Normally: It is ***absent*** in the serum, or very very low in the serum: < 20 ng / ml.
- In disease: It is ***present*** in the serum in the following conditions:

1. **Marked elevation:**
   - Hepatocellular carcinoma (HCC).
2. **Moderate elevation:**
   - Hepatitis & Cirrhosis.
   - Pancreatitis.
   - Malignancy: *GIT*, *Ovary*, *Testis*.

Normal levels of AFP do not exclude HCC

CLINICAL IMPORTANCE OF AFP

1. Follow up of cirrhotic patients for early detection of HCC.
2. Suspected cases of HCC: **e.g.** *focal hepatic lesion*.
3. After tumour resection:
   - *Early:* *to confirm successful resection.*
   - *Late:* *to detect recurrence of the tumour.*

ACUTE (FULMINANT) LIVER FAILURE

DEFINITION

- Severe hepatic failure (**rapid** deterioration of liver functions) with: *ENCEPHALOPATHY (DCL) & COAGULOPATHY (Bleeding tendency* in a patient *WITH NO PREVIOUS LIVER DISEASE.*

- **How rapid does encephalopathy and / or coagulopathy develop after the initial onset of jaundice ??** * "Jaundice to encephalopathy time"
  - Hyperacute LF: developing within *1 week*, e.g. Acetaminophen toxi
  - Acute LF: developing after *8 – 28 days*, e.g. Viral hepatitis.
  - Subacute LF: developing after *5 – 26 weeks*, e.g. Wilson's disease.

- It carries a very bad prognosis.

ETIOLOGY

- Sudden, Severe, Massive necrosis of the liver cells due to:

1. Infections:

- Viral hepatitis: All types, esp. B & D, very rare in
- Other viruses causing hepatitis: EBV, CMV, HSV, Yellow fever.

2. Drugs & toxins: "Dose – dependent"

- Alcohol.
- Halothane.
- INH, Methotrexate & *ACETAMINOPHEN.*
- Carbon tetrachloride, DDT, phosphorus.

3. OTHERS:

- Acute Budd – Chiari syndrome.
- Acute fatty liver of pregnancy.
- Reye's syndrome: *hepatic injury, CNS injury, hypoglycemia*: in child
- Wilson's disease & autoimmune hepatitis *(rare causes).*

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* O'Grady, J.G. and Williams, R. 1993. Classification of acute liver failure. *Lancet* 342: 373 – 5.

CLINICAL PICTURE

- Hepatic encephalopathy: early & severe & ends in coma.
- Fetor hepaticus.
- Jaundice: mild *in early stages* & becomes deep *in late stages*.
- Fatal course: the condition usually ends by death due to:
  - **S**evere encephalopathy & cerebral oedema.
  - **S**evere coagulopathy (bleeding tendency).
  - **S**evere septicemia.
  - **S**evere hypoglycemia.
  - **S**evere multiple organ failure: *circulatory*, *respiratory*, *renal*.

INVESTIGATIONS

1. Liver function tests:

- Plasma proteins: serum albumin is normal, but may ↓ later.
- Prothrombin time: prolonged & is used ***to assess the prognosis***.
- Serum bilirubin: ↑ & is used ***to assess the prognosis***.
- Serum transaminases: ↑ early, but may ↓ later due to massive necrosis.

2. MRI & CT of the brain: to exclude brain lesions.

3. Investigations for complications: e.g.

- Blood glucose, *Creatinine, Na, K,* ABG.

4. Investigations for the cause.

TREATMENT

1. Hospitalization in the ICU: and care of the comatosed.

2. Treatment of the cause: if possible.
3. Treatment of complications.

4. Treatment of hepatic encephalopathy: "see before".

5. Artificial hepatic support: " charcoal hemodialysis "
   - Charcoal filters are used to adsorb toxins from the blood of the patient.

6. Hepatic transplantation:
   - It is the only curative treatment for liver failure.

ASCITES

DEFINITION

- Excessive accumulation of fluid in the peritoneal cavity.

ETIOLOGY

I. TRANSUDATIVE ASCITES — *"Accumulation of transudate"*

1. **Organ failure:** — *The most common causes*
   - Liver cell failure: — *The most common cause*
   - Right sided heart failure.
2. **Portal hypertension:**
   a) *Suprahepatic causes*: RVF, Pericardial eff, High IVC obstr. & Budd-Chiari.
   b) *Intrahepatic causes*: **Liver cirrhosis**, VOD, Bilharzial periportal fibrosis.
   c) *Infrahepatic causes*: Portal vein obstr, **e.g.** thrombosis or malignancy.
3. **Hypoalbuminemia:**
   - **N**ephrotic syndrome.
   - **N**ephritic syndrome.
   - **N**utritional: *severe malnutrition* & *severe malabsorption*.
4. **Miscellaneous:**
   - **M**eig's syndrome.
   - **M**yxoedema.

II. EXUDATIVE ASCITES — *"Accumulation of exudate"*

1. **Peritoneal diseases:**
   - Infections: TB peritonitis, SBP.
   - Malignancy: Malignant deposits in the peritoneum.
2. **Pancreatic ascites:** which is a complication of pancreatitis.

III. CHYLOUS ASCITES

"*Accumulation of lymph*"

- Obstruction of the thoracic duct: tumours or filariasis.
- Rupture of the thoracic duct: trauma.

IV. HEMORRHAGIC ASCITES

"*Accumulation of blood*"

- Hemorrhagic blood diseases.
- Trauma.

CLINICAL PICTURE

1. CLINICAL PICTURE OF ASCITES

Symptoms

"*especially in tense ascites*"

- **A**bdominal **d**istension.
- **A**bdominal **d**iscomfort.
- **D**yspepsia.
- **D**yspnea.
- **D**evelopment of abdominal hernia.

Signs

Inspection

1. Abdominal distension (mainly in the flanks) ± visible veins.
2. Signs of chronic increase in the intra-abdominal pressure:
   - Subcostal angle: *widening.*
   - Umbilicus: *everted, shifted downwards, ± umbilical her*
   - Striae: *stretch marks.*
   - Divarication of the recti.
3. Dilated veins on the abdominal wall:
   - Portal hypertension (Caput Medusae).
   - IVC obstruction (Cause of ascites *or* Effect of ascites)

Palpation

1. Transmitted fluid thrill: *in tense ascites.*
2. Dipping method to feel liver & spleen: *in tense ascites.*
3. Abdominal masses may be felt: *in TB & Malignancy.*

Percussion

1. **Shifting dullness:** *is the most important clinical sign of ascites:*

Value detects moderate amount of ascites (500 ml).

Test

First step

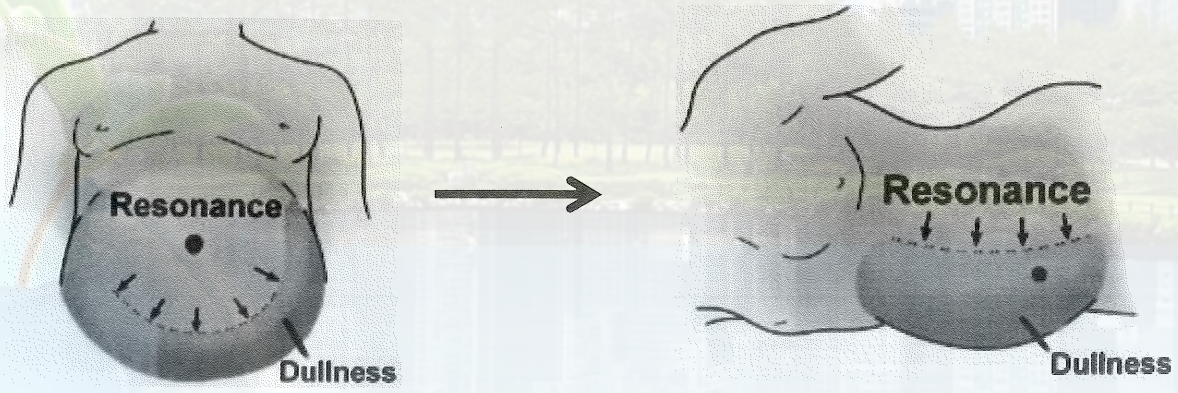
1. The patient is examined in the supine position.
2. Direct percussion is done over the abdomen, from the umbilicus to the flanks.
3. Locate the border between resonance & dullness.
4. ***Positive test:*** Percussion note is resonant over the umbilicus and dull over the flanks.

Note: The resonance over the umbilicus occurs in ascites because bowel floats to the top of the abdominal fluid at the level of the fluid surface.

Second step

5. The patient then is rolled on his side away from the examiner, and percussion from the umbilicus to flank area is repeated.
6. ***Positive test:*** When ascites is present, the area of dullness will shift to the dependent site. The area of resonance will shift toward the top.

Note: The test should be repeated on the other side.



2. **Percussion in knee-elbow position:** *for minimal ascites* (120 ml).

Auscultation

1. **Puddle sign:** *"Auscultating percussion"*

Value detects minmal amount of ascites (120 ml).

Test

1. The patient lies in the knee – elbow position.
2. Place the stethoscope on the most dependent part of the abdomen.
3. The nearby flank is percussed repeatedly by light flicking of constant intensity.
4. Gradually move the stethoscope towards the flank opposite th percussion.
5. An increase in the intensity of the sound heard by the stethoscope indicates that there is a fluid level.

2. **Venous hum:** *"heard in portal hypertension"*

- It is a soft systolic murmur over dilated para-umbilical vein.
- It is heard between the umbilicus & the xiphi-sternum.

2. SECONDARY EFFECTS OF ASCITES

a) Pleural effusion:

- It is probably due to passage of fluid through defects in the diaphragm.
- It is especially common on the right side.

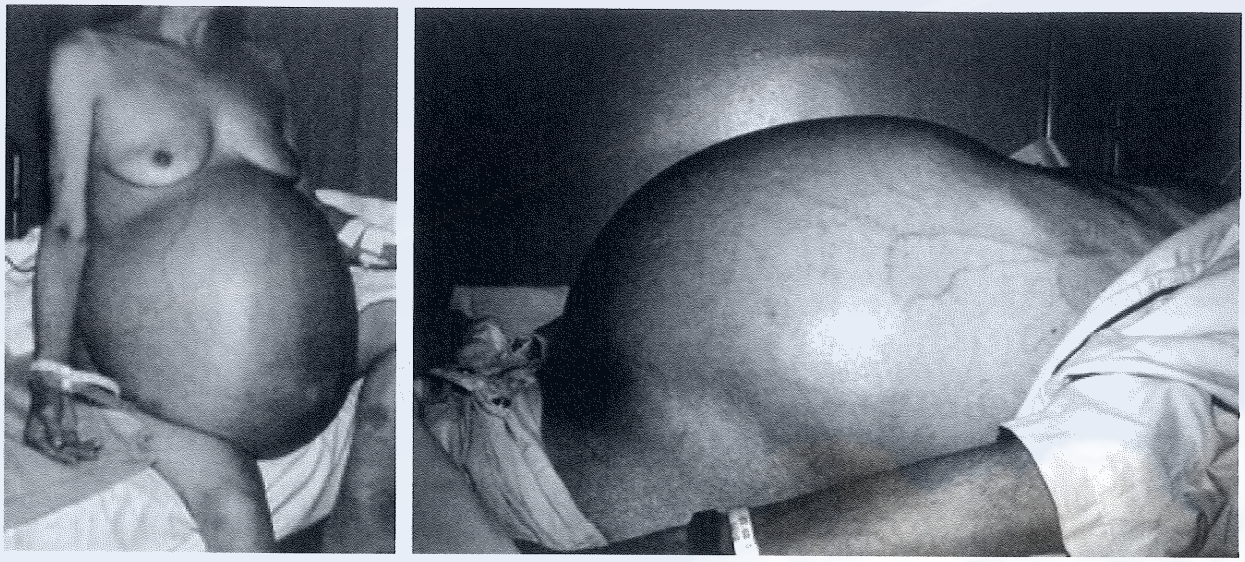
b) Signs of elevated diaphragm:

- Lung bases: diminished breath sounds & dullness.
- Cardiac apex: displaced upwards.
- Neck veins: congested pulsating neck veins.

3. FEATURES OF THE CAUSE OF ASCITES

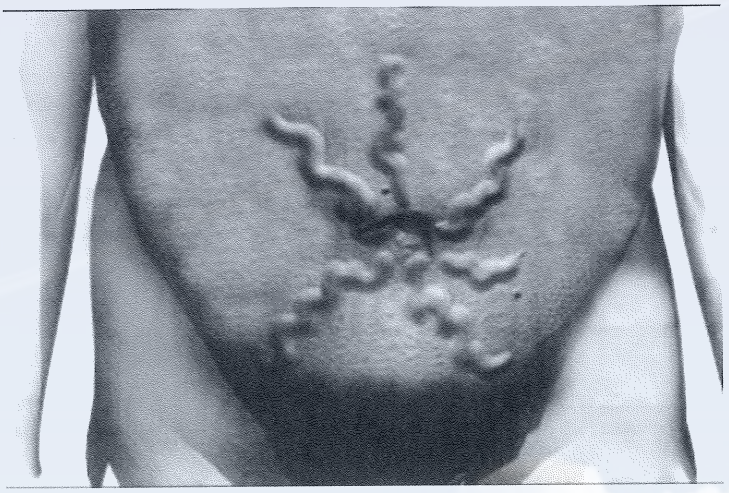
e.g. Features of liver cell failure & portal hypertension in case of **liver cirrhos**

Tense ascites with visible veins



Ascites with dilated veins

Ascites with caput medusae



Ascites with umbilical hernia

INVESTIGATIONS

I. Investigations to detect the presence of ascites:

- Abdominal ultrasonography & Abdominal CT:
  - Detect the presence of even minimal ascites.
  - Differentiate free ascites from encysted ascites.
  - Detect the cause, **e.g.** *liver cirrhosis*.

II. Investigations to detect the type of ascites:

- Aspiration of ascitic fluid:
  - Analysis for: *physical, chemical, cytological, bacteriological characters:*

a) Features of exudate & transudate effusions:

	TRANSUDATE	EXUDATE
Proteins	< 3 gm %	> 3 gm %
Fluid protein / serum protein	< 0.5	> 0.5
Specific gravity	< 1016	> 1016
LDH	< 200 IU / L	> 200 IU / L
Fluid LDH / serum LDH	< 0.6	> 0.6
Cells (WBCs)	< 1000 / cmm	> 1000 / cmm

NB Characteristics of TB effusion:

1. Exudate: rich in Lymphocytes & RBCs.
2. TB bacilli can be detected by:
   - *Staining:* *ZN stain.*
   - *Culture:* *Lowenstein-Jensen medium or BACTEC.*
   - *Animal Innoculation: Guinae pig.*

b) Features of Spontaneous Bacterial Peritonitis:

- The ascitic polymorph count exceeds 250 cells / cmm.
- The ascitic fluid culture is positive for organisms.
- The infecting organisms are usually: *gram negative organisms.*

c) Features of Hemorrhagic ascites:

- The fluid is ***bloody*** & contains many ***RBCs***.

d) Features of Chylous ascites:

- The fluid is ***milky white*** & contains many ***fat***, clears on addition of ether & stains orange with: Sudan III.

e) Features of malignant ascites: see later.

III. Investigations to detect the cause of ascites:

- For liver cirrhosis: liver function tests.
- For heart failure: echocardiography.
- For TB & malignancy: laparoscopy & biopsy.

"Recent parameter in the diagnosis of ascites"

Serum – Ascitic Albumin Gradient (SAAG)

- **Definition:**

The serum-ascitic albumin gradient (SAAG) is calculated by subtracting the albumim concentration of the ascitic fluid from the albumin concentration of a serum specimen obtained on the same day.

- **Clinical value:**

SAAG is directly related to the portal pressure:

1. Ascitic patients with SAAG ≥ 1.1 g/dl have ***portal hypertension.*** (transudative ascites)
2. Ascitic patients with SAAG < 1.1 g/dl have ***non-portal hypertension etiology.*** (exudative ascites, mostly)

DIFFERENTIAL DIAGNOSIS

A. From other causes of abdominal distension: 5 F

- **F**at: (Obesity): No shifting dullness.
- **F**latulene: Hyper-resonance all over the abdomen.
- **F**oetus: (Pregnancy): Signs of pregnancy are present.
- **F**ull urinary bladder: Suprapubic tenderness + catheter will release the urir
- **F**luid in a cyst (Ovarian cyst):
  - *Distension is mainly central.*
  - *Umbilicus is shifted upwards.*
  - *Central dullness & resonant flanks.*
  - *No shifting dullness.*

B. DD of the cause of ascites.

TREATMENT

I. Treatment of the cause of ascites.

II. Treatment of ascites in cases of liver cirrhosis:

General Rule

- Always keep the patient **W**et & **W**ise and not **D**ry & **D**rowsy.
- Treat ascites only if: mild liver failure & no encephalopathy.

A) GENERAL MEASURES:

1. **Bed rest:** better renal perfusion in recumbancy will lead to diuresis.
2. **Diet:**
   - Salt: restriction.
   - Fluid: restriction in severe cases of hyponatremia.
   - Protein: high protein diet (protein is restricted if there is encephalopathy).
3. **Follow up:**
   - Daily measurement of: urine volume & body weight.
   - Daily measurement of: electrolytes (Na & K) & renal functions.

B) MEASURES TO REMOVE THE ASCITIC FLUID:

1. **Diuretics:**
   - Indication: If weight loss is less than 1 Kg after 4 days on diet control.
   - Drugs:
     a) **At first**: K – sparing diuretics, e.g. spironolactone (100 – 400 mg/day).
     b) **If there is no improvement**: Frusemide (40 – 120 mg / day) + K supplement.
     c) **In resistant cases**: IV Mannitol or IV infusion of Dopamine.
2. **Albumin (IV):**
   - May be given to correct hypoalbuminemia.
3. **Tapping of ascites:**
   - Indication: [Tense ascites]
     - *Respiratory distress.*
     - *Impending rupture of umbilical hernia.*
   - Contra-indication: Severe liver failure, encephalopathy, renal failure.
   - Volume: 4 – 5 litres at one time combined with IV albumin.

C) TREATMENT OF REFRACTORY ASCITES:

- **Definition:**
  - Ascites unresponsive to:
    400 mg of spironolactone ***plus*** 120 mg of frusemide daily for two weeks.

- **Resistance to treatment may be due to:**
  - Lack of salt restriction: treated by adequate salt restriction.
  - Severe hypoalbuminemia: treated by IV albumin.
  - Dilutional hyponatremia: treated by fluid restriction & IV mannitol.
  - Serious problems as *SBP*, *TB peritonitis* or *malignant ascites*: ttt the cau

- **Severe terminal cases may be treated by:**
  - Le Veen shunt: (peritoneo – venous shunt)
    - *Technique:*
      - A catheter with one way valve is placed between the peritoneal cavity and the SVC to drain the ascitic fluid into the circulation.
    - *Complications:*
      - Hypervolemia, pulmonary edema, infection, DIC.
  - Transjugular intrahepatic porto – systemic shunt: (TIPS)
    - *Technique:*
      - It is an artificial channel in the liver from the portal vein to a hepatic vein to reduce the portal pressure (shunting).
        The catheter is introduced percutaneously via the IJV.
        The shunt is maintained open by a metal stent.
    - *Complications:*
      - Hepatic encephalopathy, TIPS stenosis.
  - Ascites ultrafiltration & reinfusion:
    - Ultrafiltration: removes the ascitic fluid & concentrates it.
    - Reinfusion: returns the fluid to the patient IV.
  - HEPATIC TRANSPLANTATION.

TUBERCULOUS PERITONITIS

ETIOLOGY

- Direct spread from: *TB mesenteric LN , TB enteritis, TB salpingitis.*

PATHOLOGY

- **TUBERCLES:** The peritoneum is infiltrated with miliary tubercles.
- **TYPES:**
  1. **Ascitic type:** free fluid in the peritoneal cavity with *NO ADHESIONS*.
  2. **Loculated (encysted) type:** *ADHESIONS* divide the peritoneal cavity into many loculi: each containing ascitic fluid.
  3. **Adhesive type:** *MARKED ADHESIONS* with no fluid formation.
- **TABES MESENTERICA:** TB infection of the mesenteric LN may occur.
- **THE OMENTUM:** may form a rolled (sausage – like) mass due to adhesions.

COMPLICATIONS

1. Intestinal obstruction: due to ADHESIONS.
2. Intestinal fistula.
3. Tense asites.
4. General complications of TB (refer to chest).

CLINICAL PICTURE

Symptoms

General:

- Symptoms of TB toxemia.

Abdominal:

- Constipation: is common.
- Diarrhea may occur due to: *TB enteritis, obstruction of the lacteals, Addison's disease.*
- Abdominal discomfort or pain.
- Abdominal distension.

Signs

General:

- Fever, weight loss, weakness, pallor, toxic facies.

Abdominal:

- Ascites.
- Doughy sensation, tenderness, mild rigidity.
- Palpable masses: *rolled omentum* or *tuberculous LN.*

INVESTIGATIONS

1. **Abdominal ultrasonography & Abdominal CT:**
   - Detect the presence of even minimal ascites.
   - Differentiate free from encysted ascites.
   - Detect LN enlargement.

2. **Abdominal Plain X-ray:**
   - Calcified mesenteric LN.
   - Multiple fluid levels in the loculated type.

3. **Aspiration of ascitic fluid:**
   - Straw – coloured & may be turbid.
   - Features of an exudate + increased lymphocytes + increased RBCs.
   - Detection of TB bacilli:
     - Direct smear stained with ZN stain.
     - Culture: Lowenstein-Jensen medium or BACTEC.
     - Animal inoculation in guinea pig.

4. **Laparoscopy or Laparotomy:**
   - They will show peritoneal tubercles which should be biopsied.
   - The biopsy will show the characteristic granulomatous caseous lesion of TB:
     - "Refer to the CHEST".

5. **Tuberculin test:** usually positive.

6. **PCR:** to detect mycobacterial DNA.

TREATMENT

1. **General care:** rest & proper nutrition.

2. **Specific treatment:**
   - Anti-tuberculous drugs.
   - Corticosteroids: prednisone 1 mg / Kg / day: to ↓ inflammation & fibrosis.

3. **Treatment of complications:** e.g. intestinal obstruction, tense ascites.

MALIGNANT ASCITES

ETIOLOGY

1. Secondary:
   - To abdominal malignancy: due to **direct** infiltration or **shedding** of malignant cells.
   - To extra – abdominal malignancy: due to **lymphatic** or **blood** spread.

2. Primary: tumours e.g. mesothelioma (rare).

CLINICAL PICTURE

1. Manifestations of the PRIMARY TUMOUR.
2. Features of malignant ascites: massive, rapidly re-accumulating after tapping.
3. Abdominal masses may be detected & nodules * around the umbilicus may be preser

ASPIRATION OF ASCITIC FLUID

- Features of exudate: *massive, hemorrhagic, may contain malignant cells*

TREATMENT

- Palliative:
  - Intraperitoneal injection of cytotoxic drugs.
  - Tapping of ascites in severe cases (tense ascites).

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* **Sister Mary Joseph nodule**, also called **Sister Mary Joseph sign**: a palpable nodule bulging into the umbilicus as a result of metastasis of a malignant cancer in the pelvis or abdomen.

JAUNDICE [1]

DEFINITION

- Yellow discolouration of:
  - Conjunctival membranes over the sclerae [2]
  - Skin
  - Mucous membranes

} due to ↑ bilirubin

- Jaundice is clinically detectable when: serum bilirubin exceeds 2.5 mg / dL.

TYPES

1. Hemolytic jaundice.
2. Obstructive jaundice.
3. Hepatocellular jaundice.
4. *Mixed jaundice*.

- **Important question:** **"Self – assessment"**
  "Mention some examples of a mixed jaundice".

- **Important question:** **"Self – assessment"**
  "Enumerate causes of a yellow skin".

- **Important question:** **"Self – assessment"**
  "Mention some diseases with jaundice & neurological manifestations".

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[1] Jaundice comes from the French word jaune, meaning yellow
It was once believed that patients with jaundice saw everything as yellow

[2] Bilirubin is actually deposited in the vascular conjunctiva rather than the avascular sclera

PHYSIOLOGY

1. PRE – HEPATIC (In the Blood)

- Heme molecule released as a result of RBCs destruction will eventually form:

1. **HAEMBILIRUBIN: " Unconjugated OR Indirect "**
   - It cannot be excreted through the kidney (big molecular weight & water insoluble).

2. HEPATIC (In the Liver)

- Liver cells will deal with this bilirubin through **3 steps:**

- **Uptake.**
- **Conjugation:** of bilirubin to glucuronic acid by glucuronyl transferase enzyme to form:

2. **CHOLEBILIRUBIN: " Conjugated OR Direct "**

- **Excretion:** of cholebilirubin into the bile canaliculi to reach the intestine.

3. POST – HEPATIC (In the Intestine)

- Chloebilirubin is reduced to stercobilinogen which passes in **3 routes:**

- ***Entero-hepatic circulation:*** part is absorbed to reach liver & is then re-excreted to intestine.
- ***Systemic circulation:*** part passes to systemic circ. & is excreted by kidneys as urobilinogen.
- ***Stools:*** part is oxidized into stercobilin & passes in stools giving it the brown col

PATHOGENESIS

I. HEMOLYTIC JAUNDICE:

- Increased hemolysis of RBCs ⟶ increased haembilirubin.
- The liver cannot uptake all the increased haembilirubin completely, therefore: part of haembilirubin is retained in the blood → increased serum bilirubin → **Jaundice.**
- Bilirubin is not present in urine: **" Acholuric jaundice ".**
- Excessive haembilirubin will be converted to cholebilirubin & excreted by the liver to the intestine ⟶ increased stercobilinogen ⟶ **Dark stools.**
- Increased stercobilinogen absorbed from intestine → increased urobilinogen, therefore: **Urine is normal in colour;** but darkens on standing.

II. OBSTRUCTIVE JAUNDICE:

- Biliary obstruction will prevent cholebilirubin to reach the intestine, therefore: chloebilirubin regurgitates into the blood → increased serum bilirubin → **Jaundice.**
- Excessive cholebilirubin appears in urine → **Dark urine.**
- Bile salts regurgitate into the blood & appear in urine.
- Bile does not reach the intestines → **Pale stools** (clay-coloured, bulky, offensive, greasy).
- There is decreased stercobilinogen, decreased urobilinogen.

III. HEPATOCELLULAR JAUNDICE:

- Liver cells are not able to: uptake, conjugate & excrete all the bile pigments.
- A part of haembilirubin is retained in the blood & a part of cholebilirubin regurgitates into the blood → increased serum bilirubin (direct & indirect) → **Jaundice.**
- Cholebilirubin appears in urine → **Dark urine.**
- Stercobilinogen is decreased → **Pale stools.**
- Urobilinogen is increased because the diseased liver cannot fully re-excrete the absorbed stercobilinogen.

HEMOLYTIC JAUNDICE

ETIOLOGY

- Causes of hemolytic anemia (refer to hematology).

CLINICAL PICTURE

1. Jaundice: is usually mild (lemon yellow).
2. Stools: dark.
3. Urine: normal in colour but darkens on standing.
4. Features of hemolytic anemia: e.g. HSM, gall stones, leg ulcers, hemolytic crises.
5. Features of the cause, e.g. thalassemia.

INVESTIGATIONS

1. Serum bilirubin: increased mainly the indirect.
2. Stools: increased stercobilinogen.
3. Urine: increased urobilinogen, absent bilirubin.
4. Blood picture of hemolytic anemia.
5. Investigations for the cause, e.g. Hb electrophoresis for thalassemia.

OBSTRUCTIVE JAUNDICE

(CHOLESTATIC JAUNDICE)

ETIOLOGY

I. EXTRAHEPATIC OBSTRUCTION:

1. *In the lumen*:
   - Stones in the common bile duct or common hepatic duct.
   - Ascaris worms: *very rare*.
2. *In the wall*:
   - Strictures: e.g. post-operative.
   - Tumours: e.g. cholangiocarcinoma.
3. *Pressure from outside*:
   - Cancer head of pancreas.
   - Cancer ampulla of Vater.
   - Enlarged LN in porta hepatis.

II. INTRAHEPATIC OBSTRUCTION:

1. **P**rimary biliary cirrhosis.
2. **P**regnancy jaundice.
3. **C**holestatic type of viral hepatitis.
4. **C**hronic hemolytic anemia.
5. **C**ancer liver: HCC or secondaries.
6. **C**hlorpromazine & CCPs.
7. **H**elminthes: Fasciola.
8. **H**ereditary disorders: (stasis without true obstruction)
   - *Dubin Johnson syndrome:* Hereditary defect in bile excretion with greenish black liver.
   - *Rotor syndrome:* Hereditary defect in bile excretion with normal colour of the liver.

CLINICAL PICTURE

1. Jaundice: is usually deep (olive green).
2. Stools: pale (clay-coloured, bulky, offensive, greasy).
3. Urine: dark (frothy .

4. Features of obstructive jaundice: **P**ruritus, **B**radycardia, **B**leeding tendency, **B**one affection.
5. Features of the cause, e.g. gallstones.

INVESTIGATIONS

1. Serum bilirubin: increased mainly the direct.
2. Stools: decreased stercobilinogen.
3. Urine: decreased urobilinogen, bilirubin is present.

4. Investigations suggestive of obstructive jaundice:
   - *Liver functions:* elevated enzymes (ALP, GGT, 5 – nucleotidase), prolonged PT that is corrected by parentral vitamin K. increased cholesterol with normal esterification.
   - *Ultrasonography & CT:* dilated intrahepatic biliary radicles in extrahepatic obstruction. reveals the cause of extrahepatic obstruction.

5. Investigations for the cause, e.g. MRCP, ERCP, PTC for: **detection of the site of obstruction**. Anti-mitochondrial antibodies for: **PBC**.

HEPATOCELLULAR JAUNDICE

ETIOLOGY

1. Acute: same causes of acute (fulminant) liver failure.
2. Chronic: same causes of chronic liver failure.
3. Familial hyperbilirubinemia: " ***mainly elevation of the indirect bilirubin*** "
   - **Gilbert's disease:** " ***the only common one*** "
     - It is due to a defect in the uptake & conjugation of bilirubin by the liver cells.
   - **Crigler – Najjar syndrome:**
     - It is due to a deficiency of the conjugating enzyme (glucuronyl transferase).
     - It is of 2 types: Type I (severe deficiency), Type II (moderate deficiency).
   - **Lucey – Driscoll syndrome:**
     - It is due to inhibition of the conjugating enzyme by a substance in the maternal serum.
   - **Breast milk jaundice:**
     - It is due to inhibition of the conjugating enzyme by a substance in the breast milk.

CLINICAL PICTURE

1. Jaundice: is usually moderate (orange yellow).
2. Stools: pale.
3. Urine: dark.

4. Features of liver cell failure.
5. Features of the cause, e.g. " Familial hyperbilirubinemia ":
   - They are asymptomatic, or present with mild intermittent jaundice.
   - Only Crigler – Najjar is fatal.

INVESTIGATIONS

1. Serum bilirubin: increased (direct & indirect).
2. Stools: decreased stercobilinogen.
3. Urine: increased urobilinogen, bilirubin is present..

4. Investigations of liver failure, e.g. prolonged PT that is not corrected by parentral vit. K.
5. Investigations for the cause, e.g. markers for viral hepatitis.

CLINICAL DIAGNOSIS OF JAUNDICE

A. PERSONAL HISTORTY

1. **Age:**
   - Children: hemolytic anemia, viral hepatitis.
   - Adults: calcular obstruction, viral hepatitis.
   - Old age: malignant obstruction.
2. **Sex:**
   - Females: calcular obstruction.
   - Males: malignant obstruction.
3. **Special habits:**
   - Alcohol: liver cirrhosis leading to hepatocellular jaundice.

B. PRESENT HISTORY

1. **Onset:**
   - Acute: viral hepatitis, calcular obstruction.
   - Gradual: cirrhosis, malignant obstruction.
2. **Course:**
   - Progressive: cirrhosis, malignant obstruction.
   - Regressive: viral hepatitis.
   - Intermittent: calcular obstruction, hemoylsis, Gilbert's disease, cancer ampulla of Vater.
3. **Duration:**
   - Short: viral hepatitis.
   - Long: cirrhosis (long duration will exclude malignancy).
4. **Urine:**
   - Dark: obstructive jaundice, hepatocellular jaundice.
   - Normal, but darkens on standing: hemolytic jaundice.
5. **Stools:**
   - Dark: hemolytic jaundice.
   - Pale: hepatocellular jaundice.
   - Pale + features of steatorrhea: obstructive jaundice.

6. **Fever:**
   - Viral hepatitis: pre-icteric stage.
   - Calcular obstruction: Charcot's fever *(fever, rigors, jaundice & right hypochondrial pain).*

7. **Anorexia, nausea & vomiting:**
   - Viral hepatitis: pre-icteric stage.
   - Calcular obstruction.

8. **Pain:**
   - Biliary colic: calcular obstruction.
   - Epigastric pain radiating to the back: cancer head of pancreas.
   - Dull aching pain in the right hypochondrium & epigastrium: viral hepatitis.
   - Abdominal, back, & bone pains: hemolytic crisis.

9. **Pruritus:**
   - Obstructive jaundice & maybe hepatocellular.

10. **Marked loss of weight:**
    - Malignancy.

C. PAST HISTORY

1. **B**iliary colic: calcular obstruction.
2. **B**lood transfusion & repeated injections: viral hepatitis.
3. **C**ontact with cases of viral hepatitis, or frank past history of viral hepatitis.
4. **D**rug intake: intrahepatic cholestasis, hepatitis, hemolysis.

D. FAMILY HISTORY

- Hemolytic anemia.
- Familial hyperbilirubinemia.

E. GENERAL EXAMINATION

1. **Jaundice:**
   - Mild: lemon yellow: hemolytic jaundice.
   - Deep: olive green: obstructive jaundice.
   - Moderate: orange yellow: hepatocellular jaundice.

2. **Cachexia:** in malignancy.
3. **Manifestations of hemolytic anemia:** leg ulcers & skin pigmentation.
4. **Manifestations of obstructive jaundice:** scratch marks, Xanthomata & bradycardia.
5. **Manifestations of liver cell failure:** e.g. palmar erythema & spider naevi.
6. **Skin pigmentation & clubbing:** primary biliary cirrhosis.
7. **Ecchymosis:** hepatocellular & obstructive jaundice.
8. **Oedema of lower limbs:** liver failure, & IVC obstruction by malignancy.

F. ABDOMINAL EXAMINATION

1. Liver:

- Viral hepatitis: enlarged, soft, tender.
- Cirrhosis: sharp edge & shrunken.
- Obstructive jaundice: markedly enlarged.
- Malignant liver: enlarged, hard, tender, irregular.
- Hemolytic anemia: may be enlarged.

2. Gall bladder: "*Courvoisier's law*"

- Calcular obstruction: small, tender, not palpable.
- Malignant obstruction: enlarged & palpable.

3. Splenomegaly:

- Hemolytic anemia.
- Liver cirrhosis & chronic active hepatitis.
- Viral hepatitis: sometimes.

4. Ascites:

- Liver cell failure & liver cirrhosis.
- Malignant deposits in the peritoneum.

5. Signs of portal hypertension: e.g. *dilated abdominal wall veir*

- Liver cirrhosis.

6. Abdominal masses:

- Malignancy.

INVESTIGATIONS FOR JAUNDICE

I. LABORATORY INVESTIGATIONS

A. Liver function tests

1. Hemolytic jaundice:

- Serum: Increased serum bilirubin, mainly the *indirect*.
- Stools: Increased stercobilinogen.
- Urine: Increased urobilinogen, absent bilirubin.
- Other liver function tests: normal.

2. Obstructive jaundice:

- Serum: Increased serum bilirubin, mainly the *direct*.
- Stools: Decreased stercobilinogen.
- Urine: Decreased urobilinogen, bilirubin is present.
- Others liver function tests:
  - Enzymes: elevated enzymes (ALP, GGT, 5 – nucleotidase).
  - Prothrombin time: PT: prolonged & *corrected* by parentral vitamin K.
  - Cholesterol: increased cholesterol with normal esterification.

3. Hepatocellular jaundice:

- Serum: Increased serum bilirubin, *direct & indirect*.
- Stools: Decreased stercobilinogen.
- Urine: Increased urobilinogen, bilirubin is present.
- Others liver function tests:
  - Enzymes: ALP: moderately elevated, AST & ALT: ↑ in acute cases.
  - Prothrombin time: PT: prolonged & *not corrected* by parentral vitamin K.
  - Cholesterol: normal cholesterol with decreased esterification.
  - Proteins: decreased albumin & increased globulin in chronic cases.

B. Blood Picture

- In Hemolytic jaundice: Features of hemolytic anemia.
- In Obstructive jaundice: Macrocytosis.
- In Hepatocellular jaundice: Features of anemia due to liver cell failure.

C. Serology

- In Hemolytic jaundice: Coomb's test for AIHA.
- In Obstructive jaundice: Anti-mitochondrial antibodies for PBC.
- In Hepatocellular jaundice: Antibodies for autoimmune hepatitis, hepatitis markers for VH.

II. IMAGING

1. Abdominal ultrasonography & CT

- *Biliary system:* dilated intrahepatic biliary radicles in extrahepatic obstruction.
- *Gall bladder:* stones.
- *Liver:* cirrhosis, tumours, portal vein dilatation.
- *Spleen:* splenomegaly.
- *Pancreas:* cancer head of pancreas.
- *Ascites.*

2. Visualization of the biliary system

- This is done mainly in: *extrahepatic obstruction.*
- This is done using: 3 techniques:

1. **Endoscopic Retrograde Cholangio-Pancreatography (ERCP):**
   - *Value:* visualization of the biliary system & pancreatic system.
   - *Indication:* obstructive jaundice, e.g. biliary stones or cancer head of pancreas
   - *Therapeutic use:* stone removal by sphincterotomy.
   - *Complications:* cholangitis, pancreatitis.
   - *Method:* injection of a radio-opaque substance in the biliary system by a catheter introduced through a duodenoscope.
2. **Magnetic Resonance Cholangio-Pancreatography (MRCP):**
   - Accurate visualization of the biliary & pancreatic systems.
3. **Percutaneous Transhepatic Cholangiography (PTC):**
   - *Value:* visualization of the intrahepatic bile ducts.
   - *Indication:* obstruct. jaund. to differentiate intra- from extra- hepatic obstructi
   - *Therapeutic use:* biliary drainage by a stent = PTD.
   - *Complications:* infection, hemorrhage.
   - *Method:* percutaneous injection of a radio-opaque substance into the intrahepatic bile ducts.

III. LIVER BIOPSY

- Value: diagnoses liver diseases & differentiates intra- from extra- hepatic obstructi
- Precautions: risky because of bleeding tendency & therefore PT, PC should be done first

IV. LAPAROSCOPY

- It is used for visualization of the **liver & GB** & needle biopsy could be taken.

V. LAPAROTOMY

- It is rarely used now for the diagnosis.

AMOEBIC LIVER ABSCESS

ETIOLOGY

- Hematogenous spread of Entamoeba Histolytica " *vegetative form*" from the colon to the liver through the portal vein.

PATHOLOGY

- Abscess: single, most commonly in the upper part of the right lobe.
- Abscess wall: shaggy necrotic tissue.
- Abscess contents: chocolate brown necrotic material.

CLINICAL PICTURE

Symptoms

- **Pyrexia:** fever and may be rigors.
- **Pain:** *character:* dull aching or stabbing.
  site & reference: rt hypochondrium & lower chest referred to rt shoulder & back.
  precipitating factors: coughing, straining & sneezing.
- **Pleural affection:** and may be lung affection due to spread.

Signs

- Fever: mild, it rises with secondary pyogenic infection.
- Face: pale & toxic.
- Eye: **jaundice is rare** & if present it is due to bile duct obstruction by the abscess.
- Liver: enlarged, tender, soft.
- Tenderness over the right lower ribs & intercostals spaces.

COMPLICATIONS

A. **Spread & rupture:** *may lead to:*

1. **P**ulmonary: basal consolidation or lung abscess.
2. **P**leura: *pleurisy*, pleural effusion, empyema.
3. **P**ericardium: *pericarditis* (especially in case of the uncommon left lobe abscess).
4. **P**eritoneum: *peritonitis*.
5. **S**ubphrenic: subphrenic abscess.
6. **S**kin: cutaneous amoebiasis.

B. **Secondary pyogenic infection.**

C. **Chronicity.**

INVESTIGATIONS

1. **Abdominal ultrasonography & CT:**
   - Accurate in diagnosis.
2. **Serology:**
   - Amoebic antibodies (Fluorescent Antibody Titre = FAT) can be detected in: 90 % of patients with amoebic liver abscess.
3. **Stool analysis:**
   - May show Entamoeba Histolytica: *vegetative form* OR *cyst form*.
4. **Sigmoidoscopy:**
   - May show amoebic ulcers with positive swab for amoeba.
5. **Screen & Chest X-ray:**
   - Raised right copula of the diaphragm with sluggish movement.
   - Pleural & pulmonary complications may be detected.
6. **Liver function tests:**
   - Normal (ALP: may be raised due to bile duct obstruction by the abscess).
7. **Blood picture:**
   - Polymorphnuclear leucocytosis.
8. **Therapeutic test:**
   - Metrinidazole is given & response is detected.
9. **Diagnostic aspiration:**
   - Technique: A wide-bore needle is introduced into the liver (guided by sonar or CT).
   - Aspirate: Anchovy-sauce fluid.

DIFFERENTIAL DIAGNOSIS

1. Other causes of enlarged tender liver: *congested liver* , *acute hepatitis*, *malignant liver*.
2. Other causes of fever with rigors: refer to the chapter of " fevers ".
3. Other causes of PUO: refer to the chapter of " fevers ".

TREATMENT

I. MEDICAL TREATMENT

A) Specific treatment:

1. Metronidazole (Flagyl):	750 mg	tds	orally	for	10 days.
2. Tinidazole (Fasigyn):	2 gm	daily	orally	for	5 days.
3. Emetine hydrochloride:	60 mg	daily	IM	for	10 days.

- *It has many side effects & therefore is no more used*:
  - CVS: Hypotension, HF, Arrhythmias.
  - GIT: Anorexia, nausea, vomiting, diarrhea.
  - Neurological: Peripheral neuropathy.

4. Dehydro-emetine.
5. Chloroquine: 250 mg twice daily for 20 days.

B) General treatment: rest in bed, + light nutrient diet.

C) Symptomatic treatment: analgesics & antipyretics.

D) Treatment of complications: antibiotics for secondary infection.

II. NEEDLE ASPIRATION

- It is better be guided by sonar or CT.
- It is indicated in cases not responding to medical treatment.

III. SURGICAL DRAINAGE

indicated in:

- Cases not responding to medical treatment or needle aspiration.
- Huge abscess OR multiple abscesses.
- Secondary pyogenic infection.

FATTY LIVER

DEFINITION

- Excessive deposition of fat in the liver.

ETIOLOGY

I. Alcoholic steatosis & steatohepatitis.

II. Non alcoholic steatosis & Non Alcoholic Steato Hepatitis (NASH)

- Obesity.
- Diabetes mellitus.
- Hyperlipidemia.
- Malnutrition.
- Drugs: *Corticosteroids*, *CCPs*.

III. Acute fatty liver of pregnancy & Reye's syndrome.

IV. Idiopathic.

DIAGNOSIS

1. ASYMPTOMATIC: is the RULE, *PAIN* in the right hypochondrium is the *EXCEPTION*
2. LIVER: enlarged, soft, smooth surface, may be tender.
3. Acute liver failure: may occur in case of Acute fatty liver of pregnancy or Reye's syndrome
4. Ultrasonography: bright hepatomegaly.
5. Liver biopsy: diagnostic.

TREATMENT

1. Treatment of the cause.
2. Low fat diet.

LIVER TRANSPLANTATION

INDICATIONS

- IRREVERSIBLE end-stage liver disease for which there is no acceptable alternative treatment:

  - Cirrhosis, Chronic active hepatitis, Budd-Chiari syndrome, PBC
  - Fulminant liver failure, terminal chronic liver cell failure (with terminal refractory ascites).
  - Hepatocellular carcinoma.
  - Sclerosing cholangitis.
  - Metabolic diseases: *Wilson's disease*, *Hemochromatosis*.

CONTRAINDICATIONS

- Systemic sepsis.
- Severe cardiopulmonary disease.
- AIDS.
- Metastatic malignancy.

METHODS

1. Orthotopic tranplantation:
   - The patient's liver is removed & replaced by the liver of the donor.

2. Auxiliary transplantation:
   - The patient's liver is not entirely removed.

3. Split liver transplantation:
   - The liver of the donor is split into 2 pieces so as to supply 2 patients.

4. Living donor transplantation:
   - Part of the liver of the patient's relative is transplanted.

IMMUNOSUPPRESSION

- It is done using 3 drugs:

  Cyclosprine, Prednisone, Azathioprine.

COMPLICATIONS

- Graft non-function.
- Graft rejection.
- Infection: e.g. *CMV*.
- Drug – related complications.
- Disease recurrence.

HEPATITIS

A. ACUTE HEPATITIS:

1. Infections:
   - Viral hepatitis: A, B, C, D, E.
   - Other viruses causing hepatitis: EBV, CMV, HSV, Yellow fever.

2. Drugs & toxins:
   - Alcohol.
   - Halothane.
   - INH.
   - Paracetamol.

3. Metabolic:
   - Wilson's disease.

B. CHRONIC HEPATITIS:

1. Chronic active hepatitis.
2. Chronic lobular hepatitis.
3. Chronic persistent hepatitis.

ACUTE VIRAL HEPATITIS

ETIOLOGY

- Viral hepatitis: A, B, C, D, E.
- Other viruses causing hepatitis: EBV, CMV, HSV, Yellow fever.

Hepatitis A Virus (HAV):

- Infection: Faecal – oral.
- Incubation period: 2 – 6 weeks.
- Incidence: Sporadic or epidemic.
- Age: Children & young adults.
- Acute attack: Usually mild.
- After hepatitis (sequelae): No chronicity & No relation to HCC.
- *Prophylaxis:* Vaccination or immunoglobulins.
- *Genome:* **RNA.**

Hepatitis B Virus (HBV):

- Infection: Blood, Sexual, Vertical (from mother to child).
- Incubation period: 1 – 6 months.
- Incidence: Sporadic.
- Age: Any age.
- Acute attack: Usually severe.
- After hepatitis (sequelae): Chronicity & HCC.
- *Prophylaxis:* Vaccination or immunoglobulins.
- *Genome:* **DNA.**

Hepatitis C Virus (HCV):

- Infection: Blood, Community acquired (unknown etiology).
- Incubation period: 1 – 6 months.
- Incidence: Sporadic.
- Age: Any age, but more commonly in adults.
- Acute attack: Usually mild or unnoticed.
- After hepatitis (sequelae): Chronicity & HCC.
- *Prophylaxis:* ----------
- *Genome:* **RNA.**

Hepatitis D Virus (HDV):

- Infection: Blood, Sexual, Vertical (from mother to chil

HDV is a weak incomplete virus **"Delta agent"** depending on HBsAg, *Therefore*:
- It infects only those with HBV, & there are 2 forms of infection:
  1. *Co-infection*: simultaneous infection with HBV & HDV.
     - This gives the picture of acute hepatitis which may be fulminant.
  2. *Super-infection*: super-infection of a chronic HBV carrier with HDV.
     - This causes activation of hepatitis in a previously stable patient.

- Incubation period: 1 – 6 months.
- Incidence: Sporadic.
- Age: Any age.
- Acute attack: Usually severe.
- After hepatitis (sequelae): Chronicity.
- *Prophylaxis:* Vaccination against HBV.
- *Genome:* **RNA.**

Hepatitis E Virus (HEV):

- Infection: Faecal – oral.
- Incubation period: 2 – 6 weeks.
- Incidence: Sporadic or epidemic.
- Age: Children & young adults.
- Acute attack: Usually mild except in pregnant females.
- After hepatitis (sequelae): No chronicity & No relation to HCC.
- *Prophylaxis:* ----------
- *Genome:* **RNA.**

	HAV	HBV	HCV	HDV	HEV
Infection	Oral	Blood	Blood	Blood	Oral
Faeces	Yes	No	No	No	Yes
Blood	Uncommon	Yes	Yes	Yes	No
Saliva	Yes	Yes	Yes	Unknown	Unknowı
Sexual	Uncommon	Yes	Uncommon	Yes	Unknowı
Vertical	No	Yes	Uncommon	Yes	No
IP	2 – 6 w	1 – 6 m	1 – 6 m	1 – 6 m	2 – 6 w
Incidence	Sp or epi	Sp	Sp	Sp	Sp or ep
Age	Young	Any	Any	Any	Young
Acute attack	Mild	Severe	Mild	Severe	Mild (ex
After hepatitis	No	Ch & HCC	Ch & HCC	Ch	No
Prophylax *(Act)*	Vaccine	vaccine	----------	Prevented	----------
Prophylax *(Pass)*	Immunoglobulins	Immunoglobulins	----------	By HBV vaccine	----------

CLINICAL PICTURE

A. Anicteric Hepatitis:

- They are mild cases with: no jaundice.
- They present with: *influenza – like* OR *typhoid – like* symptoms.
- They are usually missed in diagnosis.

B. Icteric Hepatitis: *3 stages*

1. Pre - icteric stage: (3 days – 2 weeks)

Symptoms

- Fever: acute onset.
- Liver: dull aching pain in the *right hypochondrium* & *epigastrium.*
- GIT: anorexia is marked especially to cigarettes, + nausea + vomiting.

Signs

- Fever: with relative bradycardia.
- Liver: enlarged, tender, soft.
- Skin: non specific rash.

2. Icteric stage: (1 – 4 weeks)

Symptoms

- Fever: drop of fever & improvement of the general condition.
- Jaundice: *Dark urine* occurs first followed by *pale stools* followed by *jaundice*.
- GIT: anorexia + nausea + vomiting markedly improve OR disappear.

Signs

- Fever: absent.
- Liver: enlarged, tender, soft.
- Spleen: slightly enlarged in 20 % of cases.
- LN: slightly enlarged LN in 10 % of cases.

3. Convalescence stage:

Symptoms

- Gradually improve, then disappear.

Signs

- Gradually improve, then disappear.

Complete recovery of the liver (clinical, biochemical & histological) may take **6 months**

SEQUELAE

A. COMPLETE RECOVERY *occurs in:*

- In most cases of: HAV & HEV.
- In many cases of: HBV & HDV.
- In few cases of: HCV.

B. COMPLICATIONS

I. Hepatic complications

1. Relapses: one of 2 forms:

- Clinical relapse: the original attack recurs & jaundice reappears.
- Biochemical relapse: serum bilirubin & enzymes rise once again.

2. Cholestatic Hepatitis: especially with HAV

- Prolonged cholestasis: pruritus, jaundice, elevated ALP.
- Persistent jaundice: for 8 – 28 weeks, followed by complete recovery.

3. Fulminant Hepatitis: massive hepatic necrosis

- Presents with: features of acute liver failure BUT is rare.

4. Post – Hepatitis Syndrome: Transaminitis

- Presents with: fatigue, anorexia, pain in the right hypochondrium.
- Investigations: all are normal EXCEPT *mild rise of transaminases*.

5. Chronic sequelae: Only in HBV, HCV, HDV

- **C**hronic hepatitis.
- **C**irrhosis: *Post – Hepatitis Cirrhosis.*
- **C**ancer: *Hepatocellular Carcinoma.*
- **C**arrier state.

II. Extra – hepatic complications

- **A**rthritis.
- **A**plastic anemia.
- **G**uillain – Barré syndrome.
- **G**lomerulonephritis (only with HBV & HCV).
- PAN & Cryoglobulinemia (only with HBV & HCV).

INVESTIGATIONS

1. Liver function tests:

- Serum bilirubin: increased, *direct* & *indirect*.
- Transaminases: increased markedly.
- ALP: increased moderately.
- Proteins: increased globulin (Gamma globulins) & normal albumin

2. Liver imaging: " Abdominal ultrasonography "

- Liver: Hepatomegaly.
- Spleen: Splenomegaly in 20 % of cases.

3. Urine analysis:

- Colour: **dark** & *frothy* due to the presence of **Bilirubin** & *Bile salts*.
- Urobilinogen: increased.
- Others: Slight *proteinuria* & *hematuria* may be present due to GN.

4. Stool analysis:

- Colour: pale with steatorrhea.
- Stercobilinogen: decreased.

5. Blood picture:

- Leucopenia with relative lymphocytosis.

6. HEPATITIS MARKERS:

A. Hepatitis " A " Markers:

- Anti – HAV antibodies: *IgM* denotes recent infection, *IgG* denotes old infection.

B. Hepatitis " B " Markers:

1. HBs Ag (Hepatitis B surface antigen):

- **Appears** 6 weeks after infection & **disappears** after 3 months.
- Persistance > 6 months indicates either: *carrier state* or *chronic state*.

2. Anti - HBs antibodies:

- Appear after 3 months & persist.
- They indicate either: *recovery* & *immunity*.

3. HBcAg (Hepatitis B core antigen):

- It is not detected in the blood, it is only detected in liver biopsy.

4. Anti - HBc antibodies:

- IgM: Acute hepatitis, persistence > 6 months indicates chronic active hepatitis.
- IgG: Carrier OR old infection.
- IgM + IgG: chronic active hepatitis

5. HBeAg:

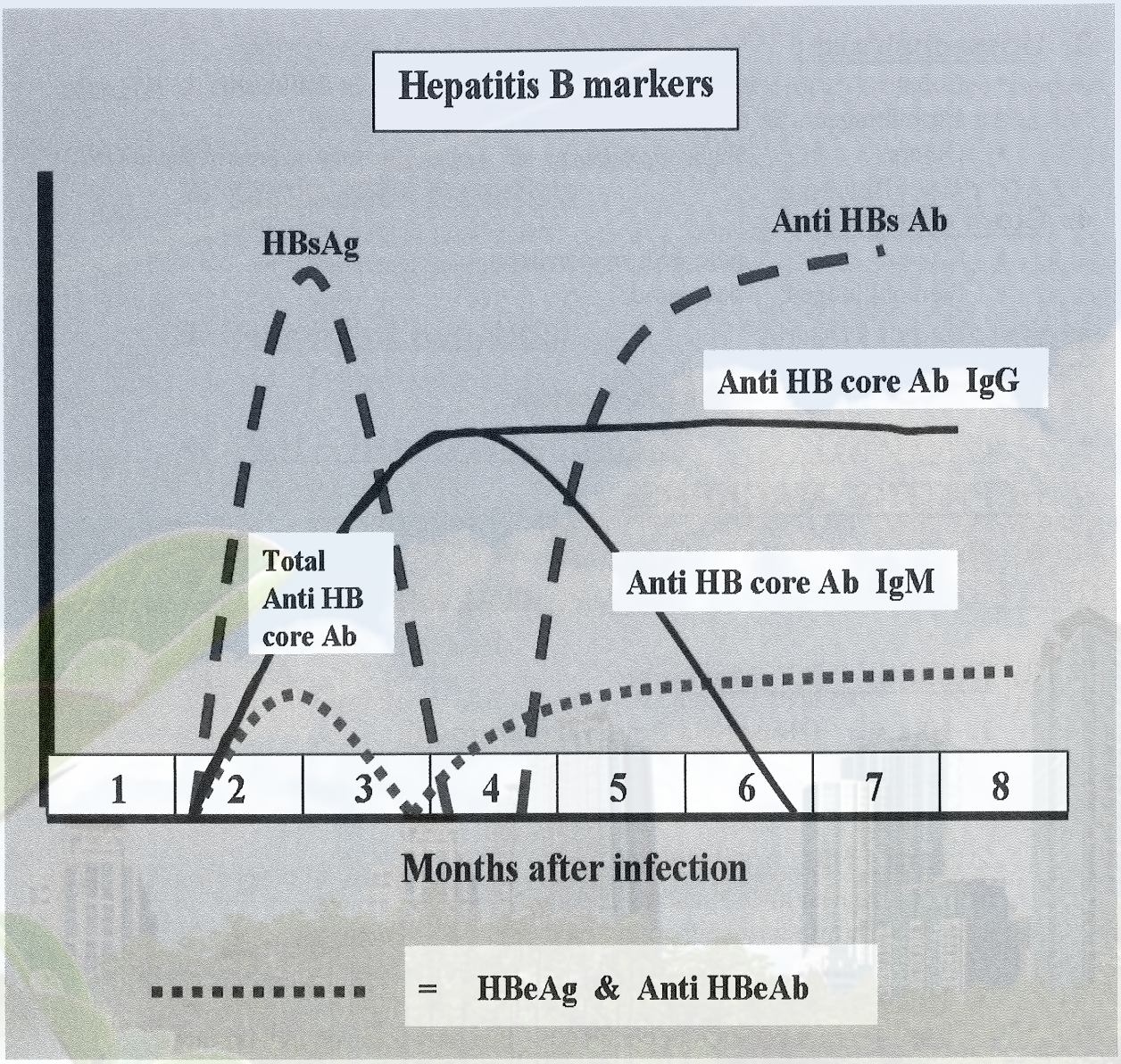
- Its presence: High infectivity.
- Its persistence > 3 months: Chronicity.

6. Anti - HBe antibodies:

- Its presence: Low infectivity.

7. PCR for HBV DNA:

- It is the most sensitive index for viral replication.


Hepatitis B markers
HBsAg
Anti HBs Ab
Anti HB core Ab IgG
Total
Anti HB
core Ab
Anti HB core Ab IgM
1
2
3
4
5
6
7
8
Months after infection
= HBeAg & Anti HBeAb

C. Hepatitis "C" Markers:

1. **Anti - HCV antibodies:** by ELISA[3] OR RIBA[4]
   - Detected after 6 weeks of infection.
2. **PCR for HCV RNA:**
   - Detected after 2 weeks of infection.

D. Hepatitis "D" Markers:

1. **Anti - HDV antibodies:**
   - IgM: recent infection.
   - IgG: old infection.
2. **PCR for HDV RNA.**
3. **HBsAG is positive.**

E. Hepatitis "E" Markers:

Anti - HEV antibodies:

- IgM: recent infection.
- IgG: old infection.

TREATMENT

1. **Bed rest:** *until:*
   - The patient is: symptom-free.
   - The liver is: no longer tender.
   - The serum bilirubin is: less than 1.5 mg / dl.
2. **Diet:**
   - Fat: restricted because they aggravate nausea.
   - Protein: given freely BUT should be restricted if liver failure develops.
   - Carbohydrates: High carbohydrate diet.
3. **Symptomatic treatment:**
   - Nausea: domperidone (anti-emetic).
   - Pruritus: cholestyramine.
4. **Treatment of complications:**
   - Cholestatic hepatitis: corticosteroids.

PROPHYLAXIS

1. Proper hygienic measures.

2. Immunoglobulins: given to exposed persons as soon as possible after exposure.

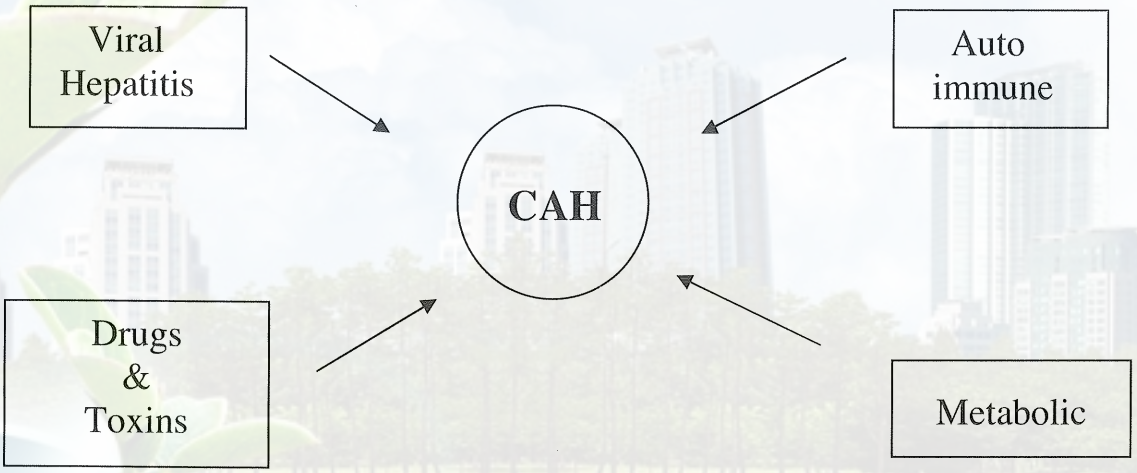
3. **H**EPATITIS B VACCINE:

   - *Types:* plasma – derived (from HBV carriers), or yeast – derived (recombinant).
   - *Efficacy:* effective response in 95 % of persons.
   - *Indication:* given to groups at **H**igh Risk for **HBV** infection including:
     - **H**ealth professionals: doctors, nurses, etc……
     - **H**emodialysis patients.
     - **H**emophiliacs & Hemolytic anemia patients.
     - **H**omosexuals & IV drug abusers.
     - Babies born to **H**BsAg positive mothers.

CHRONIC ACTIVE HEPATITIS

ETIOLOGY

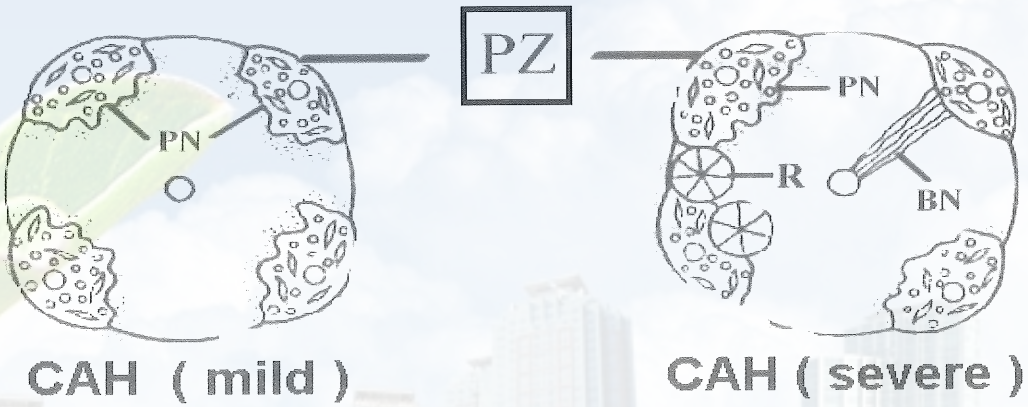
1. Viral Hepatitis: B, C, D.
2. Auto – immune : Lupoid hepatitis.
3. Drugs & toxins: Alcohol, INH, methyldopa.
4. Metabolic: Wilson's disease, alpha – 1 antitrypsin deficiency.



PATHOLOGY

1. **Mild form:**
   - Portal Zone: expanded by inflammatory infiltrate with *lymphocytes* & *plasma cells*.
   - Limiting plate: eroded (**piecemeal necrosis**), due to extension of inflammatory infiltrate into the liver lobule.

2. **Severe form:** **The previous features plus:**
   - Rosettes: fibrous septa extend into the hepatic lobules with isolation of groups of liver cells in the form of "**Rosettes**".
   - Bridging necrosis: Intrahepatic fibrous bridging (**Bridging necrosis**) occurs either: *portal – central*, or *portal – portal*, or *central – central*.
   - Cirrhosis: progression of the pathology to liver cirrhosis *is common*.



PZ = Portal Zone
PN = Piecemeal necrosis

R = Rosettes
BN = Bridging necrosis

CLINICAL PICTURE

Symptoms

- Asymptomatic: accidental discovery.
- Non – specific symptoms: fatigue, anorexia, general ill health.
- Hepatic symptoms: pain in the Rt hypochondrium, jaundice, liver failure lately.
- Extra-Hepatic symptoms: symptoms of cryoglobulinemia, GN, arthritis, etc.... may be present especially in autoimmune cases.

Signs

Hepatic signs:

- Liver: enlarged & firm.
- Spleen: enlarged.
- Signs of complications:
  - Liver cirrhosis: shrunken liver.
  - Liver cell failure & Portal hypertension: are late.
  - May be: HCC.

Extra-Hepatic signs:

- Signs of cryoglobulinemia, GN, arthritis, etc…….. may be present especially in autoimmune cases.

INVESTIGATIONS

1. Liver function tests:

- Serum bilirubin: increased, *direct* & *indirect*.
- Transaminases: increased moderately.
- ALP: increased moderately.
- Proteins: increased globulin & decreased albumin.
- Prothrombin time: prolonged.

2. Liver imaging: " Abdominal ultrasonography "

- Liver: Bright hepatomegaly.
- Spleen: Splenomegaly.

3. Liver biopsy:

A) General typical pathology of chronic hepatitis.

B) Specific pathology of the cause: e.g.

- HBV: GGA & Positive orcein stain.
- HCV: Lymphocyte deposits & Fatty changes (STEATOSIS).

4. Investigations for the cause: e.g.

- Hepatitis markers: for B, C, D.
- Auto – antibodies: for autoimmune hepatitis (ANA, ASMA, *ALKMA*).

TREATMENT

A. Treatment of HBV or HCV chronic active hepatitis:

1. Alpha – Interferon:

- *Dose:* 10 million units in HBV, & 3 million units in HCV, SC, 3 times / week, for at least 6 months.
- *Side effects:*
  - **B**ody: Fatigue.
  - **B**rain: Depression.
  - **B**M: Supression.
- *Results:* Response occurs in **30 %** of patients.

2. Pegylated Interferon: " Long acting Interferon "

- *Dose:* 180 ug, SC, once / week for at least 6 months.
- *Side effects:*
  - **B**ody: Fatigue.
  - **B**rain: Depression.
  - **B**M: Supression.
- *Results:* Response occurs in **60 %** of patients.

3. Other antiviral agents: e.g.

- Ribavirin: is added to Alpha – Interferon for HCV.
- Lamivudine: is added to Alpha – Interferon for HBV.

B. Treatment of autoimmune chronic active hepatitis:

1. **Prednisolone:** 30 mg / day for one week, then 15 mg / day for 6 months to 3 years.
2. **Azathioprine:** 50 mg / day added to prednisolone to potentiate its effect & reduce its dose.

C. Hepatic transplantation.

HEPATIC SCHISTOSOMIASIS

ETIOLOGY

1. **The ova:**
   - Schistosoma Mansoni:

     Responsible for the ***majority*** of the cases because of:
     easy access to the liver.

   - Schistosoma Haematobium:

     Responsible for the ***minority*** of the cases because of:
     difficult access to the liver through vesico-mesenteric anastomosis.

2. **Distribution:** more common in Delta region where S. mansoni is prevalent.

3. **Incidence:** more common in males, usually between 10 & 40 years.

PATHOGENESIS & PATHOLOGY

1. **The granuloma:**
   - The ova reach the liver via the portal system to induce granuloma formation in the portal tracts.
   - The granuloma is formed of: *ova* surrounded by *lymphocytes, macrophages & eosinophils*.

2. **Periportal fibrosis:**
   - The granuloma will later fibrose leading to: "periportal fibrosis" around the portal veins.

3. **Portal Hypertension:**
   - This results from periportal fibrosis.

4. **NO LIVER CELL FAILURE:**

   a) In pure Hepatic schistosomiasis:

   There is ONLY FIBROSIS, *no cirrhosis*, & *no liver cell failure*.

   b) In mixed pathology:

   Many cases of Hepatic Schistosomiasis are associated with viral hepatitis, especially HCV, (mixed pathology) resulting in: *cirrhosis* & *liver cell failure*.

CLINICAL PICTURE

Symptoms

- Early cases: asymptomatic OR symptoms of intestinal bilharziasis.

- Late cases:

1. Symptoms of Portal Hypertension:
   e.g. bleeding oesophageal varices.

2. Symptoms of Liver Cell Failure:
   a) In pure Hepatic schistosomiasis: ABSENT.
   b) In mixed pathology: PRESENT.

General Signs

1. Signs of Liver Cell Failure:
   a) In pure Hepatic schistosomiasis: ABSENT.
   b) In mixed pathology: PRESENT.
2. Signs of nutritional deficiency.
3. Signs of infantilism.
4. Signs of bilharziasis in other areas: Bilharzial cor pulmonale.

Abdominal Signs

1. Hepatomegaly: enlarged liver in early cases & shrunken liver in late cases.
2. Splenomegaly: due to portal hypertension & may reach a *HUGE size*.
3. Ascites: may develop late due to associated *HYPOALBUMINEMIA*
4. Signs of chronic increase in the intra-abdominal pressure:
   - Subcostal angle: *widening*.
   - Umbilicus: *everted, shifted downwards, ± umbilical hernia*.
   - Striae: *stretch marks*.
   - Divarication of the recti.
5. Dilated abdominal veins (Caput medusae) & venous hum may be present.

CAUSES OF ASSOCIATED HYPOALBUMINEMIA

1. Decreased intake: nutritional deficiency due to poverty.
2. Decreased absorption: malabsorption due to intestinal congestion.
3. Decreased production: due to associated cirrhosis in mixed pathology.
4. Increased loss:
   - Bleeding: Bleeding oesophageal varices.
   - Protein losing enteropathy: **C**olonic polyps & **C**ongestive enteropathy.

CLINICAL STAGES OF HEPATIC SCHISTOSOMIASIS

1. Hepatomegaly.
2. Hepatosplenomegaly.
3. Shrunken liver & splenomegaly.
4. Shrunken liver, splenomegaly & ascites.

INVESTIGATIONS

1. **Investigations for diagnosis of Schistosomiasis:**
   - **S**tool & urine analysis: Schistosoma ova.
   - **S**igmoidoscopy & biopsy: Schistosoma ova.
   - **S**erology & skin tests: Schistosoma antibodies.
   - Liver biopsy: *typical granuloma* & *periportal fibrosis*.
2. **Investigations for diagnosis of Portal Hypertension:**
   e.g. upper GI endoscopy: for oesophageal varices.
3. **Liver Function Tests:**
   a) In pure Hepatic schistosomiasis: Normal.
   b) In mixed pathology: Impaired.

   NB: Hypoalbuminemia may be present even in the absence of LCF (see the above table).
4. **Liver Imaging:** *Abdominal ultrasonography & CT.*

TREATMENT

1. Treatment of active Schistosomal infection:
   Anti-bilharzial drugs especially *Praziquantel*.

2. Treatment of Portal Hypertension.

3. Treatment of Liver cell failure: *in cases of mixed pathology.*

4. Treatment of associated viral hepatitis: *in cases of mixed pathology.*

INTESTINAL BILHARZIASIS

ETIOLOGY

The ova:

- Schistosoma Mansoni:

  Responsible for the ***majority*** of the cases because:
  They live in the mesenteric plexus of veins.

- Schistosoma Haematobium:

  Responsible for the ***minority*** of the cases:
  When vesico-mesenteric anastomosis occurs.

CLINICAL PICTURE

1. **Asymptomatic:** most of the cases.
2. **Intestinal manifestations:** *"Bilharzial dysentery"*
   - It occurs in cases of: polyps or ulcers in the colon.
   - It presents mainly with: bleeding per rectum.
   - It presents also with: chronic diarrhea & dysentery.
   - It is associated with: a mass in the left iliac fossa.
3. **Extra – intestinal manifestations:** *"Complications"*
   - Anemia of chronic disease.
   - Clubbing.
   - Hepatic Schistosomiasis.
   - Bilharzial cor pulmonale.

DEFERNETIAL DIAGNOSIS

1. Causes of bleeding per rectum.
2. Causes of chronic diarrhea.
3. Causes of dysentery.
4. Causes of a mass n the left iliac fossa.

INVESTIGATIONS

1. Investigations for diagnosis of Schistosomiasis:

- **S**tool & urine analysis: Schistosoma ova.
- **S**igmoidoscopy & biopsy: Schistosoma ova *(appear in biopsy from polyps & ulcers*
- **S**erology & skin tests: Schistosoma antibodies.
- **B**arium enema: Schistosoma polyps in the colon.
- **B**lood picture: anemia & eosinophilia.

2. Investigations for diagnosis of complications:

e.g. liver imaging for hepatic schistosomiasis.

TREATMENT

1. Treatment of active Schistosomal infection:
   Anti-bilharzial drugs especially *Praziquantel*.

2. Symptomatic treatment:
   e.g. treatment of *anemia*, antidiarrheal drugs for *diarrhea*.

3. Treatment of polyps:
   endoscopic polypectomy.

LIVER ENLARGEMENT

I. LIVER INFLAMMATION

1. *Viral:*

- Viral hepatitis: A, B, C, D, E.
- Other viruses causing hepatitis: EBV, CMV, HSV, Yellow fever.

2. *Bacterial:*

- Brucellosis.
- Typhoid.
- TB (miliary).
- Syphilis.
- Pyaemic abscesses.

3. *Protozoal:*

- Amoebic liver abscess.
- Malaria.
- Kala – azar.

4. *Helminthic:*

- Schistosomiasis.
- Hydatid cyst.
- Fasciola.

II. LIVER CONGESTION

- Right ventricular failure.
- Tricuspid valve disease (regurge or stenosis).
- Pericardial disease (effusion or constrictive pericarditis).
- High IVC obstruction.
- Budd – Chiari syndrome.
- Veno – occlusive disease.

III. LIVER CIRRHOSIS

- Cardiac & Biliary cirrhosis.
- Early stages of other causes of cirrhosis.

IV. LIVER TUMOURS

- Primary: *Benign adenoma* OR *malignant HCC.*
- Secondaries.

V. OBSTRUCTIVE JAUNDICE

- Especially extrahepatic obstruction.

VI. BLOOD DISEASES

- Anemia: *hemolytic* & *megaloblastic*.
- Polycythemia vera.
- Blood malignancies: *leukemia* & *lymphoma*.

VII. METABOLIC DISEASES

- Fatty liver.
- Hemochromatosis.
- Wilson's disease.
- Amyloidosis.
- Lipid storage diseases: *e.g. Gaucher's disease, Neimann – Pick diseas*
- Glycogen storage diseases: *e.g. Von Gierke's disease.*

VIII. MISCELLANEOUS

- Collagen diseases: *e.g. SLE.*
- Granulomatous diseaes: *e.g. Sarcoidosis.*
- Inflammatory bowel disease: *Ulcerative colitis, Crohn's diseas*

LIPID STORAGE DISEASES

- Hereditary disorders characterized by abnormal accumulation of lipids in the tissues.
- They are rare disorders affecting Jewish children.

1. **Gaucher's disease:**
   - Huge spenomegaly & moderate hepatomegaly.
   - Skin: pigmentation.
   - Bone: pains & fractures.
   - Bone marrow: characteristic *GAUCHER CELLS*.
2. **Neimann – Pick disease:**
   - Moderate splenomegaly & huge hepatomegaly.
   - Blindness, deafness, mental retardation.
   - Bone marrow: characteristic *NEIMANN – PICK CELLS*.

GLYCOGEN STORAGE DISEASES

- Hereditary disorders characterized by abnormal accumulation of glycogen in tissues.

Von Gierke's disease:

- Hepatomegaly.
- Cardiomegaly.
- Hypoglycemia.
- Short stature.

DRUG – INUCED LIVER DISEASE

1. Acute hepatitis: INH, halothane, paracetamol.
2. Chronic hepatitis: INH, methyl dopa.
3. Cirrhosis: INH, methyl dopa, amiodarone, methotrexate.
4. Cholestasis: CCPs, Chlorpromazine.
5. Fatty liver: Corticosteroids, CCPs.
6. Tumours: CCPs, Androgen.
7. VOD: Cyclophosphamide.

HEPATIC TUMOURS

I. BENIGN TUMOURS:

e.g. Hepatocellular adenoma.

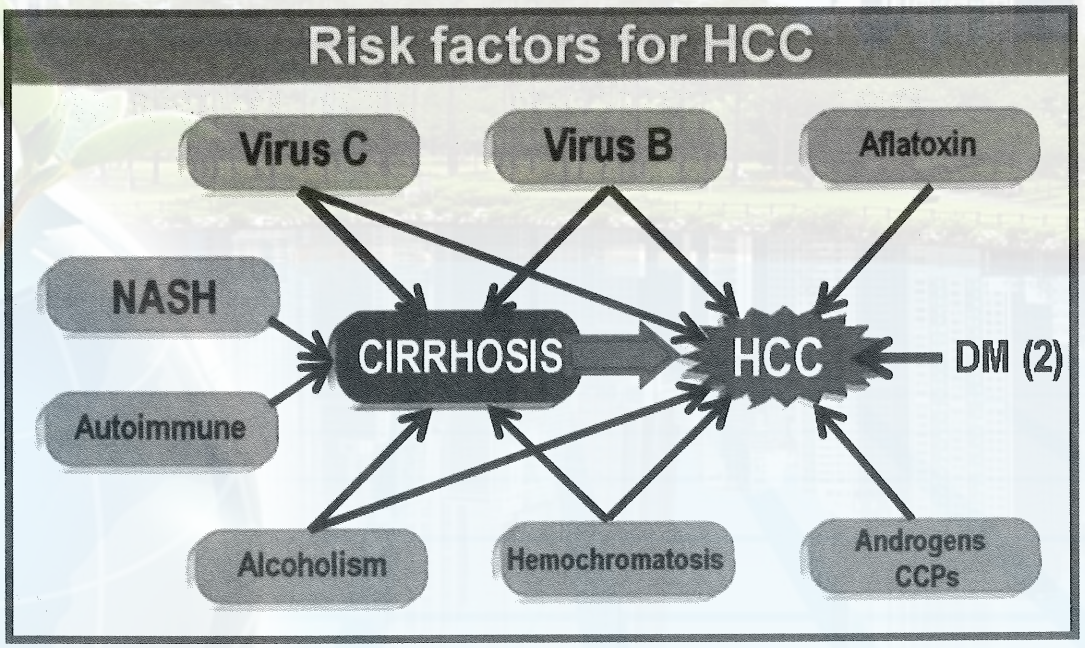
II. MALIGNANT TUMOURS:

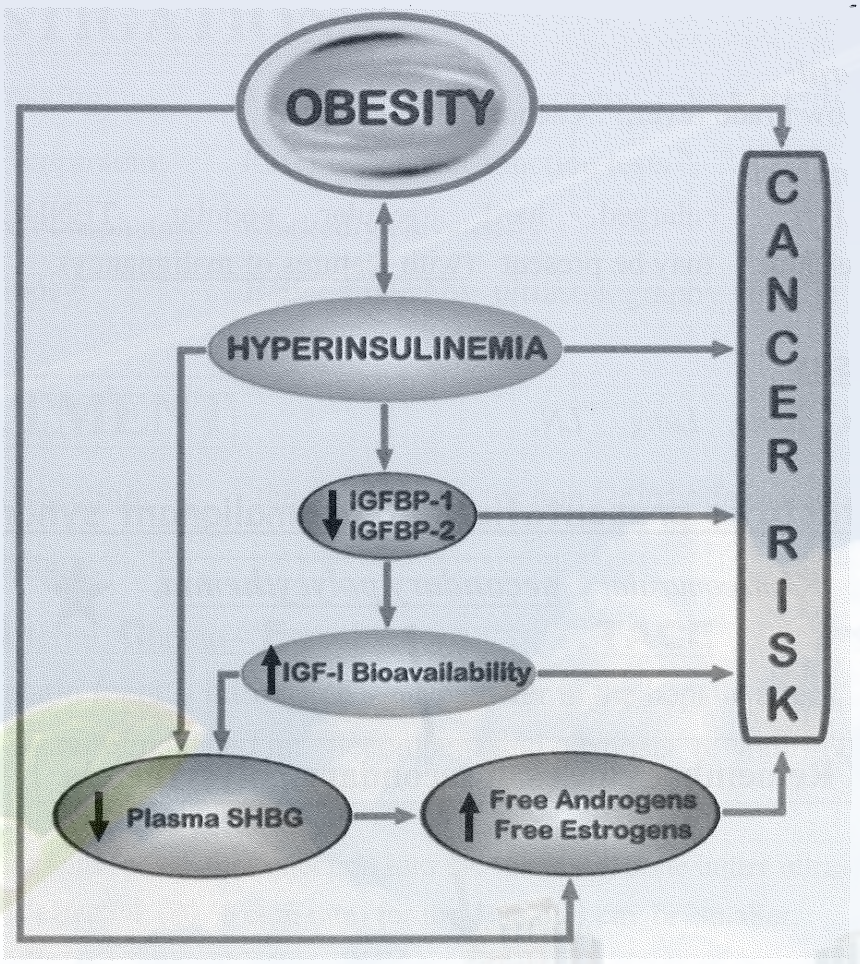
- Primary: Hepato Cellular Carcinoma (HCC) = Hepatoma.
- Secondary: Metastases.

HEPATOCELLULAR CARCINOMA

INCIDENCE

1. Age: usually over 40.
2. Sex: more in males.
3. Predisposing factors:
   - CIRRHOSIS: especially *post-Virus*, *Hemochromatosis*, *Alcoholic*.
   - Viruses: B, C.
   - Hemochromatosis.
   - Alcoholism.
   - Aflatoxin: a fungus metabolite that contaminates stored food.
   - Androgenic steroids: and also CCPs (estrogen).
   - DIABETES (TYPE 2): probably due to ..... ???





CLINICAL PICTURE

Symptoms

1. Asymptomatic: accidental discovery during ultrasonography or CT scan.
2. Pain: dull aching pain in the right hypochondrium.

Criteria to suspect HCC in a patient with Liver cirrhosis

1. **R**apid deterioration of the condition.
2. **R**efractory ascites and encephalopathy.
3. **R**ight hypochondrial pain or appearance of a local swelling.

Signs

General:

Low grade fever, cachexia, jaundice.

Abdominal:

Liver: enlarged, hard, irregular, nodular, TENDER.

Ascites: may be present (with features of malignancy).

Metastases

Brain, Bone, Lung, LN.

Non-metastatic presentations (Paramalignant syndrome)

e.g. Gynecomastia, secondary polycythemia. ★

Remember causes of secondary polycythemia

ETIOLOGY

A) Secondary polycythemia:

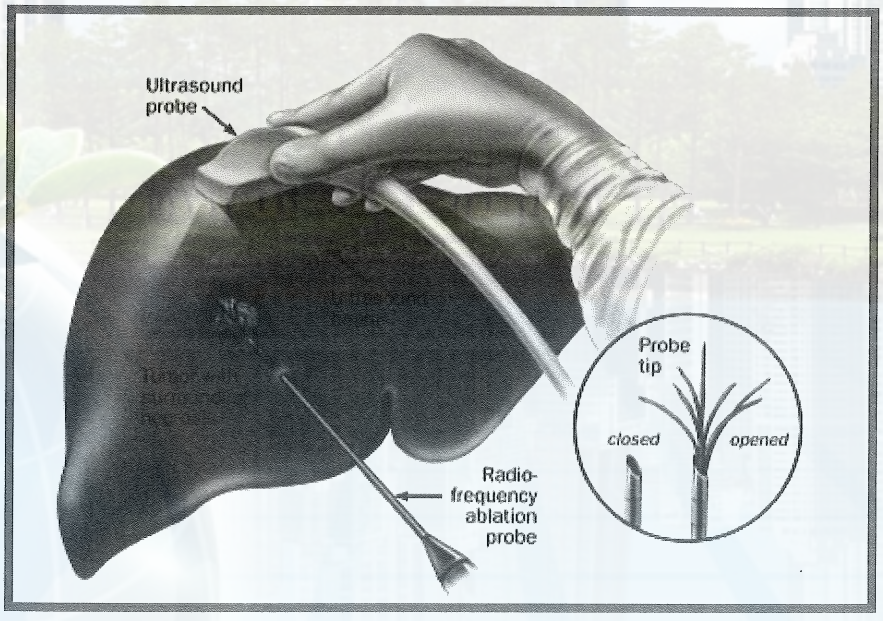
1. **Chronic hypoxia** (e.g. COPD & other causes of chronic central cyanosis).
2. **Cushing's syndrome & prolonged corticosteroid therapy.**
3. **Renal disease** (e.g. hypernephroma & hydronephrosis) → ↑ EPO.
4. **Paramalignant syndrome** (e.g. HCC). ★
5. **Dehydration** → hemoconcentration (false polycythemia).

INVESTIGATIONS

1. **L**iver imaging: Abdominal ultrasonography, CT, MRI, Isotopic scanning.
2. **A**lpha Fetoprotein: Refer to " Liver function tests ".
3. **A**lkaline Phosphatase: Markedly elevated.
4. **L**iver biopsy: Better guided by ultrasonography or CT.

TREATMENT

1. Surgical resection: the ttt of choice for non – cirrhotic patients.
2. Chemotherapy.
3. **T**rans **A**rterial **C**hemo – **E**mbolisation: **TACE**
   - Gelatin foam is introduced via a catheter in the hepatic artery.
   - It is contraindicated in: decompensated cirrhosis & multifocal HCC.
4. Percutaneous ablation:
   - Percutaneous ethanol injection into the tumour is done under ultrasound guidance.
   - It is effective (80 % cure rate) for tumours of 3 cm or smaller.
   - **Radiofrequency ablation (RFA)**, using a probe inserted into the tumour under ultrasound guidance is an alternative (causes more tumour necrosis).
5. Hepatic transplantation.



Radiofrequency ablation (RFA) in hepatocellular carcinoma

IMPORTANT POINTS FOR MCQs

- HCC is the most common primary liver tumour.
- HCC is the 6th most common cause of cancer world – wide.
- Chronic hepatitis B infection increases the risk of HCC 100 – fold.
- Chronic hepatitis B infection is the major risk factor for HCC world – wide.
- HCC risk is 4 times higher in HBeAg – positive than HBeAg – negative cases.
- Cirrhosis is present in 75 – 90 % of cases with HCC.
- HCC risk is higher in males and rises with age.

MALABSORPTION

DEFINITION

- Defective absorption of *any* or *all* of the food components absorbed from the intestine.
- The main defect in absorption involves: *FATS*, leading to steatorrhea " fatty stools ".

ETIOLOGY

I. IMPAIRED DIGESTION

1. **G**astric causes:
   - **G**astric surgery: e.g. gastrectomy.
   - **G**astric carcinoma: *decreased HCL* → bacterial overgrowth in the intestine.
   - **G**astrinoma: *increased HCL* → inhibition of pancreatic lipase.
2. Pancreatic causes:
   - **C**hronic pancreatitis.
   - **C**ystic fibrosis of the pancreas (mucoviscidosis).

II. REDUCED BILE SALTS

1. Hepatic causes:
   - Acute & chronic hepatitis.
2. Biliary causes:
   - Obstructive jaundice.

III. SMALL INTESTINAL DISEASES:

1. **A**myloidosis.
2. **B**acterial overgrowth: *" Stagnant (blind) loop syndrome "*
   - **S**trictures **D**iverticulosis, **D**iminished motility (e.g. **D**M).
3. **C**oeliac disease: *" Gluten – sensitive enteropathy "*
4. **D**isaccharidase deficiency:
   - Lactase deficiency → malabsorption of lactose → bloating & diarrhea.

5. **Ileal resection:** *" short bowel syndrome "*

6. **Infections:**
   - TB.
   - Tropical sprue.
   - Whipple's disease.
   - Parasites: e.g. *Giardia Lamblia*.

7. **Irradiation enteritis.**

8. **Inflammation:**
   - Crohn' disease.

9. **Lymphatic obstruction:**
   - Lymphoma.

IV. DRUG - INDUCED

1. Cholestyramine.
2. Neomycin.
3. Dendivan.

V. MISCELLANEOUS

1. Heart: Congestive heart failure & Constrictive pericarditis.
2. Thyroid: Myxoedema.

CLINICAL PICTURE

I. General features of malabsorption:

- Steatorrhea: stools are *bulky*, *greasy*, *offensive*, *difficult to flush*.
- Diarrhea.
- Abdominal distension, colics, borborygmi (audible intestinal sounds).

II. Specific features of malabsorption:

- Specific clinical features according to the *deficiency of specific factors*.
- See the following table:

Deficiency of specific factors

- **Fats:** Loss of weight.
- **Proteins:** Muscle wasting & nutritional oedema.
- **Carbohydrates:** Hypoglycemia.

- **Vitamin A:** Night blindness.
- **Vitamin D:** Rickets or osteomalacia.
- **Vitamin E:** Dermatitis.
- **Vitamin K:** Bleeding tendency that is corrected by parentral vitamin K.

- **Vitamin B_1:** Beri – Beri.
- **Vitamin B_2:** Glossitis & angular stomatitis.
- ***Nicotinic acid*:** Pellagra.
- **Vitamin B_6:** Peripheral neuropathy.
- **Vitamin B_{12}:** Megaloblastic anemia & SCD.
- ***Folic acid*:** Megaloblastic anemia.

- **Iron:** Microcytic anemia.
- **Sodium:** Muscle cramps & hypotension.
- **Potassium:** Myopathy & arrhythmias.
- **Calcium:** Parasthesia & tetany.
- **Magnesium:** Parasthesia & tetany.

- **Water:** Dehydration.

III. Features of the cause:

1. Coeliac disease " Gluten – sensitive enteropathy "

- ***Etiology*:** ***Unknown***
  - Unexplained sensitivity to "gluten" which is a protein present in wheat & barley.
  - Unexplained mucosal damage by "gliadin" which is a fraction of "gluten".

- ***Clinical picture*:**
  - Age: most commonly 20 – 40 years.
  - Presentation: severe malabsorption syndrome + dermatitis herpetiformis.
  - Associations: other autoimmune diseases, e.g. *autoimmune thyroiditis* & *IDDM*.
  - Complications: increased incidence of *lymphoma* & *small intestinal carcinoma*.

- ***Investigations*:**
  - Jejunal biopsy: Villous atrophy (***the most important investigation***).
  - Serology: IgA antigliadin Ab, IgA anti-endomysial Ab, **IgA anti-tTG Ab**.
  - General investigations for malabsorption.

- ***Treatment*:**
  - Withdrawal of all gluten from the diet: gluten – free diet.
  - Corticosteroids or immunosuppressive drugs: in refractory cases (no response to diet).

2. Tropical sprue

- ***Etiology:*** ***Unknown***
  - May be bacterial infection.
- ***Clinical picture:***
  - Severe malabsorption, especially of: fats, folic acid & cobalamin.
  - Associated mouth ulcers.
- ***Investigations:***
  - Jejunal biopsy: Villous atrophy (***the most important investigation***).
  - General investigations for malabsorption.
- ***Treatment:***
  - Antibiotic: Tetracycline 250 mg / 6 hours orally daily.
  - Replacement: Folic acid & cobalamin.

3. Whipple's disease

- ***Etiology:*** ***Unknown***
  - Infection.
- ***Clinical picture:***
  - Steatorrhea.
  - Fever, arthritis, lymphadenopathy, cranial nerve affection.
- ***Investigations:***
  - Jejunal biopsy: heavy infiltration by *macrophages*.
  - General investigations for malabsorption.
- ***Treatment:***
  - Antibiotic: Trimethoprim – sulfamethoxazole.

INVESTIGATIONS

I. Investigations to diagnose malabsorption:

1. Fat in the stools:

- Normally: fat in the stools is not more than 7 gm / day.
- In steatorrhea: total fat is increased:
  - Non – split: in *impaired digestion.*
  - Split: in *small intestinal diseases.*

2. Urinary D – Xylose test:

- Method: give 25 gm D – Xylose orally, then collect urine over the next 5 hours.
- Normally: urine collected over 5 hours should contain at least 5 gm of D – Xylose.
- In steatorrhea: urine collected over 5 hours will contain less than 5 gm of D – Xylose
  " provided that renal functions are normal ".

3. Barium follow through of the small intestine:

- Loss of the normal feathery appearance of the jejunum.
- Segmentation & flocculation of the barium.
- Dilatation of the intestinal lumen.

} Malabsorption pattern

4. Jejunal Biopsy:

- *Recently:* taken through the enteroscope.
- *Previously:* taken by the intestinal biopsy capsule.

II. Investigations to diagnose the cause:

1. Glucose tolerance test:

- In small intestinal diseases: flat curve.
- In pancreatic causes: diabetic curve.

2. Tests for Bacterial overgrowth:

♥ **^{14}C – Xylose breath test:**

- *Method:* measure the $^{14}CO_2$ in the breath after oral administration of ^{14}C – Xylose.
- *In bacterial overgrowth:* $^{14}CO_2$ in the breath will increase because more bacteria will act on the ^{14}C – Xylose.

♥ **Culture of the jejunal aspirate:**

- *This is done using a sterile polyethylene tube.*

III. Investigations for the deficient factors:

1. Blood picture: microcytic or megaloblastic anemia.

2. Plasma proteins: hypoproteinemia.

3. Serum electrolytes: diminished *Iron*, *Na*, *K*, *Ca*, *Mg*.

4. Bone X – ray: osteomalacia.

TREATMENT

1. Treatment of the cause: e.g. anti – TB drugs for TB.
2. Replacement of the deficient factors: e.g. parentral *vitamins* & *minerals*.

GIT BLEEDING

HEMATEMESIS

DEFINITION

- Vomiting of blood.

ETIOLOGY

I. Oesophageal causes:

1. Bleeding oesophageal varices.
2. GORD: causes oesophageal erosions.
3. Cancer oesophagus.
4. Mallory – Weiss syndrome: tear of the oesophago – gastric junction due to *severe vominting*.
5. Rupture of aortic aneurysm into the oesophagus.

II. Gastro - duodenal causes:

1. Acute gastritis: due to drugs, especially aspirin,, NSAIDs, corticosteroids.
2. Acute gastric ulcer: due to "*drugs*", especially aspirin, NSAIDs, corticosteroids, OR due to severe stress "*Stress ulcer*".
3. Chronic peptic ulcer: gastric ulcer OR duodenal ulcer.
4. Bleeding gastric varices: fundal varices.
5. GORD: associated with hiatus henia.
6. Cancer stomach: and cancer ampulla of Vater.
7. Peutz – Jeghers syndrome: GI polyposis & muco – cutaneous pigmentation.
8. Angiodysplasia of the stomach.

III. Upper small intestinal causes:

1. Angiodysplasia of the small intestine.
2. Familial polyposis: adenoma.
3. Cancer: adenocarcinoma.
4. Ulcers: secondary to *drugs as NSAIDs* OR *typhoid ulcers*.

IV. General causes:

1. Hemorrhagic blood diseases: purpura, hemophilia & leukemia.
2. Hemorrhagic fevers: plague.
3. Hypertension: severe hypertension.

V. False hematemesis:

- Vomiting of ingested blood coming from: *bleeding nose*, *mouth* OR *pharynx*.

DIFFERENTIAL DIAGNOSIS

- Differentiation from hemoptysis: *refer to the chest.*
- Differentiation from false hematemesis: *by local examination.*
- DD of the cause of hematemesis through:
    1. Clinical picture.
    2. Investigations:
        - Upper endoscopy & enteroscopy.
        - Barium meal & follow through.
        - Liver function tests & abdominal ultrasonography.
        - Angiography & isotopic studies.

TREATMENT

- Treatment of the cause.

MELENA

DEFINITION

- Passage of black tarry stools due to the presence of digested blood.

ETIOLOGY

- Same causes of hematemesis.

DIFFERENTIAL DIAGNOSIS

- DD of dark stools:
    1. *Intake of iron.*
    2. *Hemolytic anemia.*
- DD of the cause of hematemesis.

TREATMENT

- Treatment of the cause.

BLEEDING PER RECTUM

ETIOLOGY

- Piles: the most common cause.
- Cancer rectum OR colon: the most serious cause.
- Inflammatory bowel disease: especially UC.
- Intestinal bilharziasis.
- Anal fissure.
- Bacillary dysentery.
- Colonic polyps: familial polyposis.
- Diverticulitis.
- TB of the colon.

TREATMENT

- Treatment of the cause.

DIARRHEA

DEFINITION

- Passage of increased amounts of loose stools.

PATHOGENESIS

1. Osmotic diarrhea

- **Cause:**
  - Presence of high concentration of non – absorbed hypertonic substances (**heavy osmotic load**) in the intestine which will attract fluid from the blood to the intestine → loose stools.
- **Examples:**
  - In malabsorption syndrome: high concentration of nutrients & solutes.
  - In disaccharidase deficiency: high concentration of lactose.
  - Ingestion of non – absorbable substances, e.g. *lactulose*.

2. Secretory diarrhea

- **Cause:**
  a. ↑↑ active intestinal secretions of fluid & electrolytes.
  b. ↓↓ intestinal absorption of fluids.
- **Examples:**
  a. ↑↑ active intestinal secretions of fluid & electrolytes:
     - Enterotoxins: e.g. Cholera & E.coli.
     - Hormones: e.g. Vaso – active intestinal peptides " VIPs ".

  b. ↓↓ intestinal absorption of fluids:
     - Malabsorption syndrome.

3. Inflammatory diarrhea "Mucosal destruction"

- **Cause:**
  - Damage to the intestinal mucosa will cause loss of *fluid* & *blood*, and will also ↓↓ the ability of the intestine to absorb *fluid* & *nutrients*.
- **Examples:**
  - Bacillary dysentery.
  - Inflammatory bowel disease, e.g. *Ulcerative colitis*.

4. Motility – related diarrhea:

- **Cause:**
  - Hypermotility → defective absorbtion of *fluid* & *nutrients*.
- **Examples:**
  - Thyrotoxicosis.
  - Post – vagotomy.

CAUSES OF ACUTE DIARRHOEA

I. INFECTION

A. *Bacterial:*

1. Shigella: *Bacillary dysentery*.
2. Salmonella.
3. Campylobacter.
4. Cholera.
5. E. coli.
6. Food poisoning: *salmonella*, *staph.* & *clostridium*.

B. *Viral:*

1. Rota virus.
2. Norwalk virus.
3. Adenovirus.
4. Enterovirus.

C. Protozoal:

1. Entamoeba Histolytica.
2. Giardia Lamblia.
3. Malignant malaria.
4. Balantidium coli.

D. Helminthic:

1. Ascaris.
2. Ankylostoma.
3. Strongyloides stercoralis.

II. TOXIC

1. Arsenic.
2. Lead.
3. Mercury.

III. DIETARY

1. High fiber diet: *Excessive intake of cellulose*.
2. Food allergy.

IV. NERVOUS

- Emotional stress: e.g. *Irritable bowel syndrome*.

V. MISCELLANEOUS

1. Appendicitis.
2. Ischemic colitis.

CAUSES OF CHRONIC DIARRHEA

A. Diseases of the colon:

1. **A**moebic colitis.
2. **A**IDS: *due to opportunistic infections*.
3. **B**ilharzial colitis.
4. **C**ancer colon.
5. **C**rohn's disease of the colon **or** ulcerative colitis.
6. **D**iverticulosis.

B. Diseases of the small intestine:

- Same causes of intestinal malabsorption.

C. Endocrinal causes:

1. Diabetic neuropathy.
2. Thyrotoxicosis.
3. Addison's disease.
4. Carcinoid *syndrome*.
5. Zollinger – Ellison *syndrome*: "Gastrinoma".
6. Verner – Morrison *syndrome*: " Pancreatic cholera ":
   - A pancreatic tumour which secretes VIPs causing secretory diarrhoea.

D. Drugs:

1. Antacids: H_2 – receptor antagonists, PPI.
2. Anti – inflammatory drugs: NSAIDs, Colchicine.
3. Anti – arrhythmic drugs: Quinidine.
4. Anti – neoplastic drugs: Busalfan.
5. ANTIBIOTIC – ASSOCIATED DIARRHEA: ***Pseudomembranous colitis***,
   - It occurs with any antibiotic especially: **Clindamycin** & Cephalosporin
6. LAXATIVE ABUSE.

E. Miscellaneous:

1. Obstructive jaundice.
2. Pellagra.
3. Vitamin B_{12} deficiency.

INTESTINAL AMOEBIASIS

ETIOLOGY

- **Organism:**
  - Protozoon: Entamoeba Histolytica "*cyst form*"
- **Transmission:**
  - Fecal – oral route.
- **Mode of infection:**
  - Ingestion of the cyst which resists gastric acidity & is transformed into "*vegetative form*" in the intestine & then passes to the colon.

NB: Amoebiasis is the 3rd leading parasitic cause of death worldwide surpassed only by: ------- & -------.

CLINICAL PICTURE

1. ASYMPTOMATIC

- This occurs in most cases (~ 90 %).
- They pass cysts in the stools & cause spread of infection (CARRIER).

2. ACUTE AMOEBIC DYSENTERY

- Acute diarrhea: frequent motions, may be 10 motions per day.
- Stools: *mucus*, *blood* & may be *pus* in secondary infection.
- Associated features: colics, tenesmus, pain & tenderness over caecum & sigmoid.
- General condition: GOOD, No fever, No toxemia, No dehydration.

3. CHRONIC AMOEBIC COLITIS

- Chronic diarrhea: recurrent attacks of diarrhoea.

COMPLICATIONS

1. Intestinal:

- Amoebic ulcers: which may rarely perforate.
- Amoeboma: **mass in the right iliac fossa** → intestinal obstruction.

2. Extra – intestinal:

- Invasion of the colonic mucosa leads to dissemination of the organism to extracolonic sites, predominantly the LIVER.

- LIVER: *Amoebic hepatitis* & *Amoebic liver abscess.*
- Brain abscess.
- Pulmonary infection.
- Genitourinary infection.

INVESTIGATIONS

1. Serology:

- Amoebic antibodies may be detected in the serum of the patient.

2. Stool analysis:

- May show Entamoeba Histolytica: *vegetative form* or *cyst form*.

3. Sigmoidoscopy:

- May show amoebic ulcers with positive swab for amoeba.
- Ulcers: *flask – shaped ulcers* with *healthy mucosa inbetween*.

DIFFERENTIAL DIAGNOSIS

1. From other causes of: *acute diarrhea.*
2. From other causes of: *chronic diarrhea.*
3. From other causes of: *dysentery.*
4. From other causes of: *mass in the right iliac fossa..*

TREATMENT

A) SPECIFIC TREATMENT:

1. Luminal amoebicidals: "for ttt of cysts"

- Indication: for treatment of asymptomatic cyst passers.
- Drugs:
  - Furamid: 500 mg tds orally for 10 days.
  - Paromomycin: 500 mg tds orally for 10 days.
  - Iodoquinol: 650 mg tds orally for 20 days.

2. Tissue amoebicidals: "for ttt of vegetative form"

- Indications:
  - Acute intestinal amebiasis: amoebic dysentery.
  - Extra – intestinal amebiasis: amoebic liver abscess.
- Drugs:
  - Emetine hydrochloride: 60 mg daily IM for 10 days.
    - *It has many side effects & therefore is no more used*:
      - CVS: Hypotension, HF, Arrhythmias.
      - GIT: Anorexia, nausea, vomiting, diarrhea.
      - Neurological: Peripheral neuropathy.
  - Chloroquine: effective ONLY in amoebic liver abscess, (250 mg twice daily for 20 days).

3. Tissue & luminal amoebicidals:

- Indications:
  - Acute intestinal amoebiasis: amoebic dysentery.
  - Chronic amoebic colitis.
  - Extra – intestinal amoebiasis: amoebic liver abscess.
- Drugs:
  - Metronidazole: 750 mg tds orally for 10 days.
  - Tinidazole: 2 gm daily orally for 5 days.

B) SYMPTOMATIC TREATMENT:

- Drugs: Antispasmodic drugs, Antidiarrheal drugs.

DYSENTERY

DEFINITION

A disease characterized by:

- INTESTINAL: *frequent watery stools*, *blood & mucus in the stools*, *tenesmus*.
- GENERAL: *fever*, *dehydration*.

CAUSES

1. **A**moebic dysentery.
2. **B**acillary dysentery.
3. **B**ilharzial dysentery.
4. **C**ancer colon ***or*** cancer rectum.
5. **C**rohn's disease of the colon ***or*** ulcerative colitis.
6. **D**iverticulosis.
7. **P**rotozoa: Malaria ***or*** Giardia Lamblia.
8. **P**oisoning: Mercury poisoning.
9. UREMIC DYSENTERY.

TENESMUS

DEFINITION

A disease characterized by:

- During defecation: ***painful*** straining.
- After defecation: sense of ***incomplete rectal evacuation*** + ***persistent desire*** to defecate.

CAUSES

- **I**rritable bowel syndrome.
- **I**nflammatory bowel disease: e.g. *Ulcerative Colitis*, *Crohn's Disease*.
- **I**nfective colitis: e.g. *Bacillary Dysentery*.
- **Rectal** prolapse.
- **Rectal** carcinoma.
- Causes of Dysentery.

BACILLARY DYSENTERY

ETIOLOGY

- **Organism:**
  - Gram negative Shigella: *S. dysenterie*, *S. flexneri*, *S. boydii*, *S. sonnei*.
- **Transmission:**
  - Fecal – oral route.

CLINICAL PICTURE

- Acute diarrhea: frequent motions, may be 15 motions per day.
- Stools: **watery**, with excessive *pus*, *blood* & *mucus*.
- Associated features: colics, tenesmus, pain & tenderness over caecum & sigmoid.
- General condition: **BAD**, fever, toxemia, dehydration.

COMPLICATIONS

- Blood: bacteremia.
- Bone: osteomyelitis & arthritis.
- Eye: iridocyclitis & conjunctivitis.
- Kidney: UTI.

INVESTIGATIONS

1. **Stool analysis:**
   - Excessive WBCs & RBCs.
   - Culture demonstrates the organism.
2. **Sigmoidoscopy:**
   - Inflammation: generalized inflammation of the colon.
   - Membrane: dirty yellowish pseudomembrane which bleeds when removed.

TREATMENT

A) SPECIFIC TREATMENT:

1. Correction of dehydration:
   - Excess *oral fluids* & *IV fluids* in severe conditions.

2. Antibiotic treatment:
   - Ciprofloxacin 500 mg bid orally for 5 days.

B) SYMPTOMATIC TREATMENT:

1. Antispasmodic drugs: *for severe abdominal colics.*

2. Antidiarrheal drugs:
   - SHOULD NOT BE GIVEN because:
     They may decrease the intestinal motility and thus decrease the clearance of bacteria, leading to more deterioration.

GORD

DEFINITION

- Clinical symptoms due to abnormal gastro – oesophageal reflux.

ETIOLOGY & PATHOGENESIS

- **Normally:**

  Occasional episodes of gastro – oesophageal reflux are common in health.

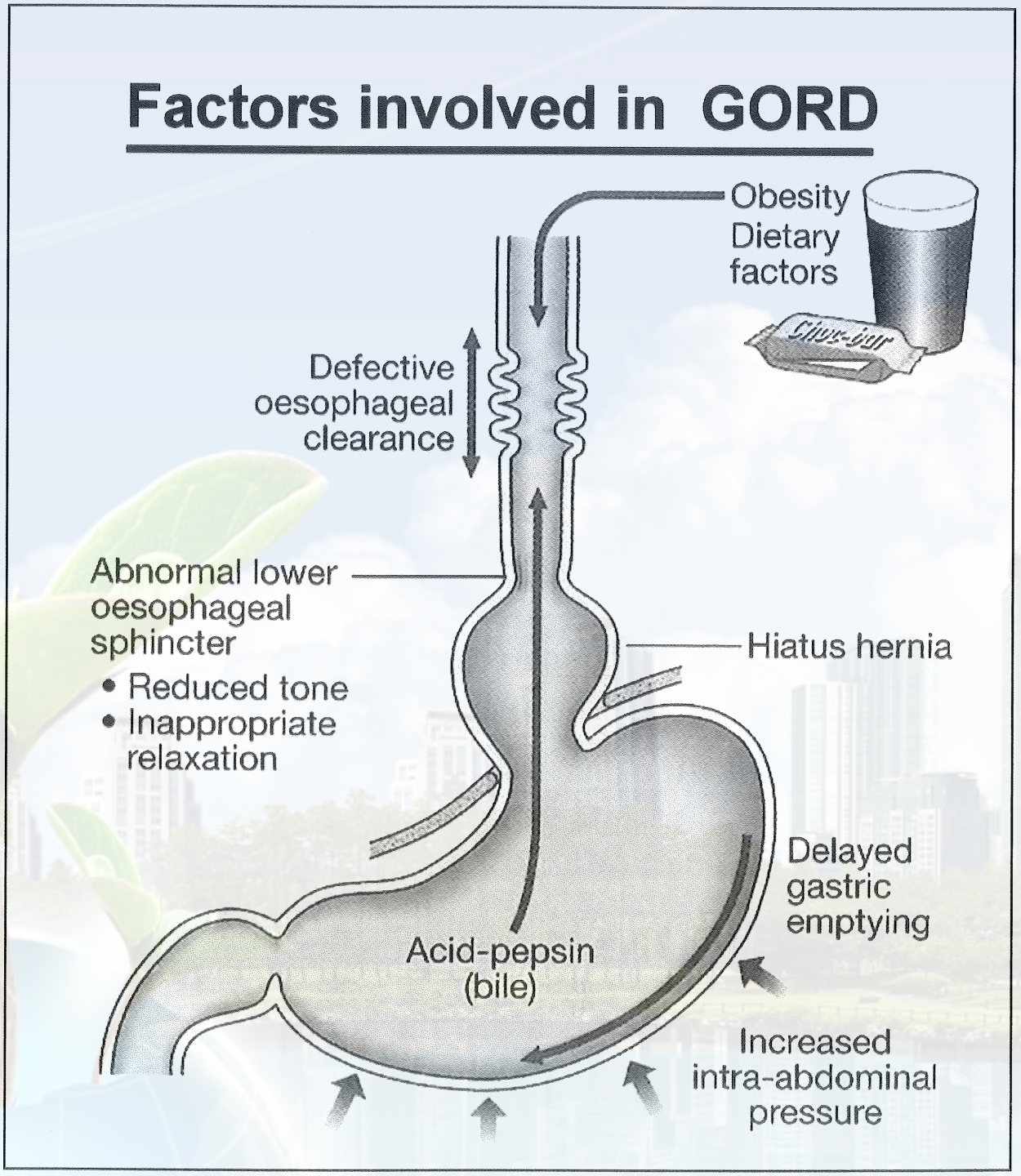
  Reflux is normally followed by oesophageal peristaltic waves which efficiently clear the oesophagus, also, alkaline saliva neutralizes the residual acid and therefore, symptoms do not occur.

- **GORD:**

  Symptoms will occur if: the oesophagus is exposed to gastric contents for prolonged periods of time, resulting in symptoms and, in some cases, **oesophagitis**.

  Several factors are known to involved:

  1. Abnormalities of the LOS: (Failure of anti – reflux mechanism)
     - Reduced tone of the LOS.
     - Frequent episodes of inappropriate LOS relaxation.
  2. DYSMOTILIY:
     - *Oesophagus:* poor oesophageal peristalsis leading to failure of acid clearance.
     - *Stomach:* delayed gastric emptying leading to increased chance for reflux.
  3. Increased intra – abdominal pressure:
     - *Pregnancy*.
     - *Obesity*.
  4. HYPERACIDITY: gastric acid is the most important oesophageal irritant.
  5. HIATUS HERNIA.
  6. DIETARY FACTORS: (e.g. fat, chocolate, alcohol, coffee)
     - Relax the LOS and may provoke symptoms


Factors involved in GORD
Obesity
Dietary factors
Defective oesophageal clearance
Abnormal lower oesophageal sphincter
• Reduced tone
• Inappropriate relaxation
Hiatus hernia
Delayed gastric emptying
Acid-pepsin (bile)
Increased intra-abdominal pressure

CLINICAL PICTURE

1. **Heart burn:** The major feature of GORD.
2. **Pain:**
   - **Site & reference:** "epigastric, retrosternal," radiating to:
     - Shoulders, arms & back.
   - **Character & duration:**
     - Compressing or burning.
     - Variable duration.
   - **Precipitated by:**
     - Bending, straining, lying down.
   - **Relieved by:**
     - Antacids.
     - Sometimes by nitrates.
   - **Associated symptoms:**
     - Waterbrash.
3. **Dysphagia & Odynophagia:**
   - This may be associated with regurgitation of food & acid into the mouth.
4. **Hematemesis & melena:**
   - This is due to mucosal inflammation and / or ulceration.

COMPLICATIONS

A) Chest complications:
- Chronic cough.
- Aspiration pneumonia.
- Nocturnal asthma (due to regurgitation & aspiration).

B) Other Complications:
- Oesophagitis: which (if longstanding) may cause oesophageal stricture.
- Barrett's oesophagus: mucosal metaplasia (pre – malignant).
- Iron deficiency anemia: due to repeated bleeding.

DIFFERENTIAL DIAGNOSIS

- From other causes of acute chest pain especially *angina* & *MI*.

INVESTIGATIONS

- GORD is essentially a CLINICAL DIAGNOSIS.
- Many patients are be treated without investigations.

1. Oesophagoscopy:

- It may show: oesophagitis.

2. Barium swallow:

- It may show: hiatus hernia.

3. 24 – hour intraluminal pH monitoring:

"The most important investigation"

- It shows the number of reflux episodes occurring over 24 hors.
- It is often combined with: *manometry*.

TREATMENT

I. MEDICAL TTT

A) *Specific treatment:*

1. Alginates: they ↑ pH.
2. Antacids: they coat the mucosa, ↑ pH, ↓ reflux.
2. H_2 – receptor antagonists: e.g. Ranitidine.
3. **Proton pump inhibitors:** e.g. Omeprazole, "*drugs of choice*".
4. Prokinetic drugs: e.g. Metochlopramide ↑ the peristalsis.

B) *General treatment:*

1. Diet control & Weight reduction.
2. Raising the head of the bed during sleeping.

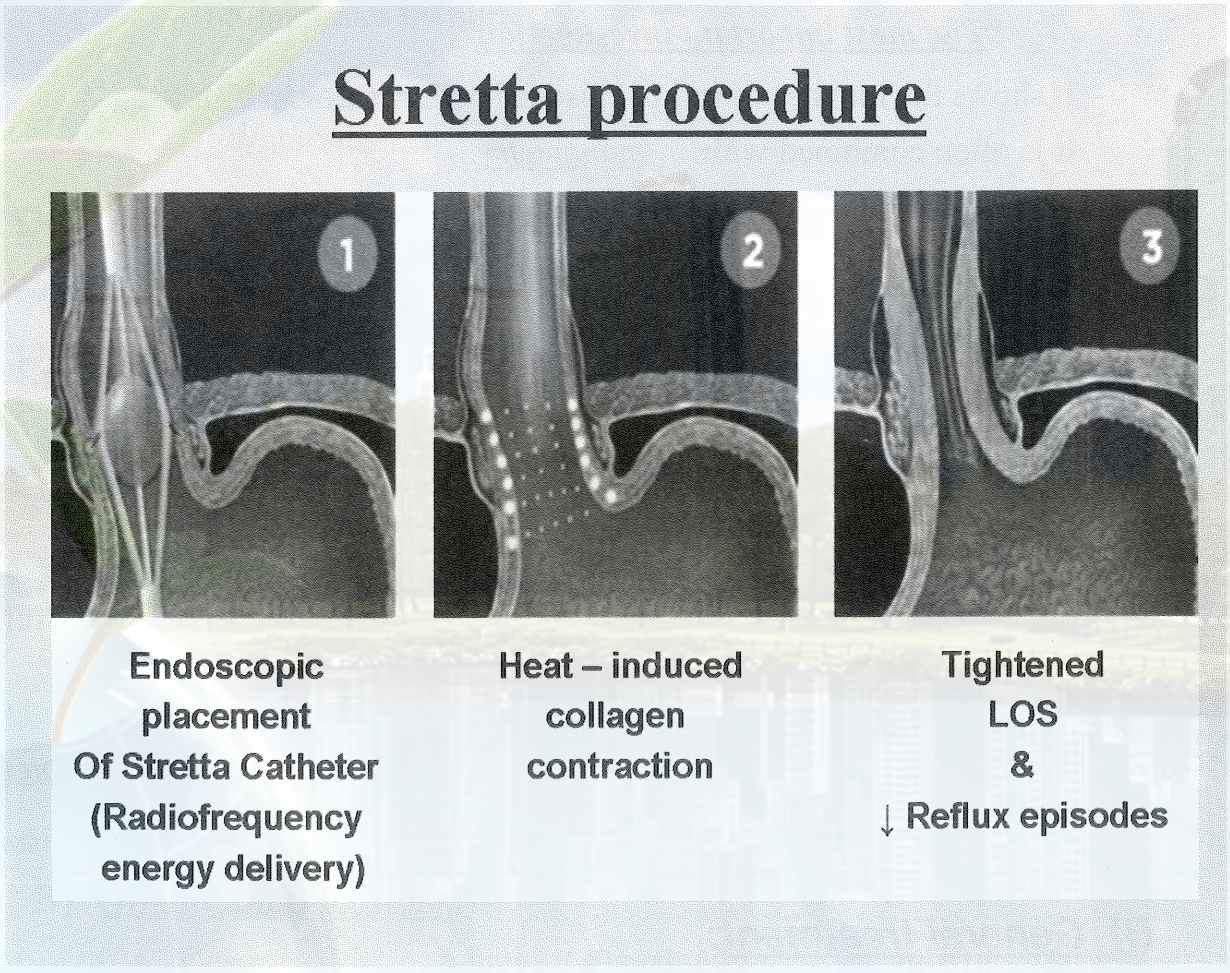
II. SURGICAL TTT

A) *Standard surgical ttt:*

- Nissen fundoplication: in para – oesophageal HH, or failed medical ttt.
- The procedure is now routinely performed laparoscopically.

B) *Other ttt:* (FDA approved)

- Endoscopic anti – reflux surgical procedures:
  1. Endocinch procedure.
  2. Stretta procedure.



CAUSES OF ACUTE ABDOMEN

Surgical causes

1. Acute appendicitis.
2. Acute cholecystitis.
3. Acute pancreatitis.
4. Acute intestinal obstruction.
5. Acute salpingitis OR twisted ovarian cyst.
6. Colic: *biliary*, *renal*, *intestinal*.
7. Perforated peptic ulcer.

Medical causes

1. Acute myocardial infarction.
2. Acute pleurisy & Pneumonia.
3. Diabetic ketoacidosis.
4. Uremia.
5. Hemolytic crisis.
6. FMF.
7. Food poisoning.
8. Rheumatic fever (non – infective peritonitis).
9. SLE.

GASTRITIS

Inflammation of the gastric mucosa; it may be: ACUTE or CHRONIC.

ACUTE GASTRITIS

Inflammation of the **SUPERFICIAL** gastric mucosa.

ETIOLOGY

1. DRUGS:
   - Aspirin, NSAIDs, Iron preparations.
2. **S**TRESS (Stress gastritis):
   - **S**epsis, **S**hock, **S**troke (or AMI), **S**evere burns (Curling's ulcer).
3. INFECTIONS:
   - CMV, HSV.

CLINICAL PICTURE

- Asymptomatic: discovered accidentally at upper endoscopy.
- Symptomatic: anorexia, N, V, dyspepsia, heart burn, hematemesis & melena.

INVESTIGATIONS

Upper endoscopy confirms the diagnosis.

TREATMENT

1. Removal of the offending cause.
2. Drugs:
   - *H_2 receptor antagonists (ranitidine 150 mg bid).*
   - *Proton pump inhibitors (omeprazole 20 mg once daily).*

CHRONIC GASTRITIS

ETIOLOGY

1. Chronic active gastritis: Helicobacter pylori.
2. Autoimmune gastritis: Pernicious anemia.
3. Infections: CMV, TB.
4. OTHERS:
   - Crohn's disease.
   - Chemical gastritis:
     - Repeated chemical injury, **e.g.** ***bile reflux*** or ***chronic NSAIDs*** ingestion.

CLINICAL PICTURE

- Asymptomatic: discovered accidentally at upper endoscopy.
- Symptomatic: anorexia, N, V, dyspepsia, heart burn, hematemesis & melena.

INVESTIGATIONS

- Upper endoscopy confirms the diagnosis.
- Investigations of the cause, e.g. **H. pylori:**
  - *Serology:* *specific antibodies.*
  - *Biopsy:* *through an endoscopy.*
  - *Breath tests:* *known as urea breath tests.*

TREATMENT

- Treatment of the cause: e.g. **H. pylori:**

Triple therapy (1 – 2 weeks, orally, twice daily)

1. PPI e.g. omeprazole: 20 mg
2. Clarithromycin: 500 mg.
3. Amoxicillin: 1000 mg.

INFLAMMATORY BOWEL DISEASE

DEFINITION

The term **IBD** refers to the: IDIOPATHIC chronic **I**nflammatory **B**owel **D**iseases including:

- ULCERATICE COLITIS (UC).
- CROHN'S DISEASE (CD).

ETIOLOGY

UNKNOWN ..... some ***theories*** were suggested:

1. **I**mmunological: presence of associated extra-intestinal autoimmune manifestations.
2. **I**atrogenic: prolonged use of NSAIDs.
3. **I**nheritance: genetic factors.
4. **I**ngested food: milk, complex carbohydrates.
5. **I**nfection: by atypical mycobacteria (unproven theory).

INCIDENCE

- Age: young (20 – 30 years).
- Sex: more in females.
- Stress: is a precipitating factor.
- Smoking: protects against UC, BUT: is associated with CD.

ULCERATIVE COLITIS

DEFINITION

A chronic inflammatory disorder of the mucosa of the colon.

PATHOLOGY

1. Site: " Diffuse, Continuous, Superficial inflammation of the MUCOSA only "

- Proctitis: affection of the rectum only.
- Left-sided colitis: affection of the rectum + distal colon.
- Total colitis: affection of the rectum + whole colon.

Proximal spread

2. Lesion:

- Multiple ulcerations.
- Multiple CRYPT ABSCESSES: *infiltration of the crypt lumen by excessive neutrophils.*

CLINICAL PICTURE

I. INTESTINAL MANIFESTATIONS

A. Acute attack:

- Bleeding per rectum: is the most important feature.
- Diarrhoea with mucopus: may occur more than 10 times daily.
- Tenesmus.
- Lower abdominal pain: colicky.

B. Chronic disease:

- After recovery from the acute attack, the patient returns to a normal bowel habit.
- Then the disease runs a chronic intermittent course characterized by:
  - Acute exacerbations: precipitated by **N**SAIDs or **N**ervous stress.
  - Remission periods: which may be very short & thus need continuous ttt.

II. EXTRA - INTESTINAL MANIFESTATIONS

Extra - Intestinal Manifestations of UC

1. *General:*	Fever	+	general constitutional manifestations.
2. *Nutritional:*	Anemia	+	manifestations of vitamin deficiency + PLE.
3. *Eye:*	Conjunctivitis	+	iridocyclitis.
4. *Skin:*	Erythema nodosum	+	pyoderma gangrenosum + vasculitis.
5. *Joints:*	Arthritis.		
6. *Liver & GB:*	Gall stones	+	autoimmune hepatitis.
7. *Kidney:*	Oxalate stones.		
8. *Lungs:*	Interstitial pulmonary fibrosis.		

COMPLICATIONS

1. Hemorrhage.
2. Perforation.
3. Megacolon: acute (toxic) dilatation of the colon.
4. Malignancy: increased risk in cases of "***total colitis of 10 years duration***".

INVESTIGATIONS

1. Stool analysis & culture:

- To exclude an infective colitis.
- Presence of: *WBCs, RBCs due to inflammation.*

2. COLONOSCOPY:

- Lesion: diffuse inflammation, mutiple ulcerations, friable mucosa.
- Biopsy: multiple CRYPT ABSCESSES.

3. Barium enema:

- Lead - pipe appearance: loss of haustrations + narrowing of the lumen.

4. Blood tests:

- Anemia, Leucocytosis.
- Abnormal liver function tests.

TREATMENT

I. MEDICAL TREATMENT

A. ACUTE ATTACK:

1. Steroids: "*the most important ttt for the acute attack*"

- Prednisone, orally 1 mg / Kg / day: in acute attacks.
- Hydrocortisone IV 100 mg / 6 hours: in severe attacks (for 5 days).
- Hydrocortisone retention enema: in severe proctitis.

2. Salicylates:

- Sulphasalazine (sulpha + salicylates): 1 gm / 6 hours orally.
- Mesalamine (5 – aminosalicylic acid): 1 gm / 6 hours orally.

3. Symptomatic ttt:

- Anti-diarrheal agents: for severe diarrhoea.
- Antibiotics: for severe secondary bacterial infection.

B. RESISTANT CASES:

- Immunosuppressives: Azathioprine or Cyclosporine may be beneficial.

C. MAINTENANCE :

- Sulphasalazine: 2 gm orally daily for 2 years.
- Mesalamine: 2 gm orally daily for 2 years.

II. SURGICAL TREATMENT

Indications:

1. Failure of Medical ttt.
2. Development of severe complications.
3. Total colitis for more than 10 years: *because of high cancer risk*.

Operation:

The standard operation is: " Proctocolectomy with permanent ileostomy ".

CROHN'S DISEASE

DEFINITION

A chronic inflammatory disorder which affects:

- Any part of the GIT from the mouth to the anus.
- The whole thickness of the bowel wall: " *Transmural* ".

PATHOLOGY

1. Site:

- The TERMINAL ILEUM and RIGHT COLON are most commonly involved.

2. Lesion:

- Thickening & narrowing of the affected bowel.
- Ulcers, fissures, fistulas, abscesses.
- SKIP LESIONS: areas of normal bowel inbetween the lesions.

CLINICAL PICTURE

I. INTESTINAL MANIFESTATIONS

- Acute colicky pain & tenderness: in the right iliac fossa (simulating acute appendicitis).
- Mass: in the right iliac fossa.
- Malabsorption syndrome: diarrhoea, steatorrhoea, loss of weight.
- Intestinal obstruction.
- Colonic CD: features similar to UC.

II. EXTRA - INTESTINAL MANIFESTATIONS

- Same as Ulcerative Colitis.

COMPLICATIONS

Same as Ulcerative Colitis, BUT:

- Malignancy: is less common in CD.
- Fissures, Fistulas, Abscesses: are more common in CD.

INVESTIGATIONS

1. Stool analysis & culture:

- To exclude an infective colitis.
- Presence of: *WBCs, RBCs due to inflammation*.

2. COLONOSCOPY & ILEOSCOPY:

- Lesion: diagnoses the characteristic pathology & detects colonic affection.
- Biopsy: differentiates between CD and UC.

3. Barium enema:

- To detect colonic affection.

4. Barium follow-through:

- Deep ulcerations.
- String sign: areas of narrowing.
- SKIP LESIONS: areas of normal bowel inbetween the lesions.

5. Blood tests:

- Anemia, Leucocytosis.
- Abnormal liver function tests.

TREATMENT

I. MEDICAL TREATMENT

A. ACTIVE ILEITIS:

- Prednisone: orally 1 mg / Kg / day.
- Immunosuppressives: Azathioprine & Cyclosporine may be beneficial in resistant cases.

B. ACTIVE COLITIS:

- Prednisone: orally 1 mg / Kg / day.
- Immunosuppressives: Azathioprine & Cyclosporine may be beneficial in resistant cases.
- Sulphasalazine (sulpha + salicylates): 1 gm / 6 hours orally.

C. ANAL DISEASE :

- Metronidazole: 800 mg tds orally.

II. SURGICAL TREATMENT

Indications:

1. Failure of Medical ttt.
2. Development of severe complications.
3. Failure of growth in children.

Operation:

- Standard: Limited resection with end to end anastomosis.
- In severe colitis: Proctocolectomy with permanent ileostomy.

INTESTINAL TUBERCULOSIS

ETIOLOGY

- ***Secondary:*** *to pulmonary TB* *(Human bacilli).*
- ***Primary:*** *ingestion of infected milk* *(Bovine bacilli).*

PATHOLOGY

- The most common affected site is the ***ileo-cecal region***.

CLINICAL PICTURE

- General Symptoms: *night fever, night sweating, loss of appetite, loss of weight.*
- Abdominal Symptoms: *abdominal pain, diarrhoea,* ***MALABSORPTION SYNDROME***.
- Signs: *abdominal tenderness, mass in the right iliac fossa.*

NB Evidence of Pulmonary TB may be present.

COMPLICATIONS

- Bleeding.
- Perforation.
- Fistula.
- Obstruction.
- General complications of TB (refer to Chest).

DIFFERENTIAL DIAGNOSIS

- *Crohn's disease.*
- *Causes of Malabsorption syndrome.*

INVESTIGATIONS

- Enteroscopy or colonoscopy and biopsy: *for pathological diagnosis*.

TREATMENT

- Anti- Tuberculous drugs.

IRRITABLE BOWEL SYNDROME

DEFINITION

A group of abdominal symptoms for which no organic cause can be found.

ETIOLOGY

1. Motility disturbances: ↑ or ↓ strength of colonic motility.
2. Psychological disturbances: evidence of stress, depression, or anxiety.

CLINICAL TYPES

1. Spastic colitis: chronic abdominal pain & constipation.
2. Diarrhoea: chronic intermittent watery diarrhea.
3. Alternating type: alternating constipation & diarrhea.

CLINICAL PICTURE

1. PAIN:

- Character & site: chronic crampy pain in any part of the colon, esp. the left iliac fossa.
- Precipitating & relieving factors: ↑ after meals or stress & ↓ by passage of flatus or stools.

2. TENDERNESS:

- Over the left iliac fossa: and the spastic sigmoid colon may be palpable.

3. IRRITABLE MOTIONS:

- Chronic constipation, or diarrhoea, or both.
- **Ribbon-like stools** with sense of incomplete evacuation (Tenesmus).

4. IRRITABLE PERSONALITY:

- Features of anxiety or stress may be present.

DIAGNOSIS

Diagnosis of IBS is essentially a CLINICAL DIAGNOSIS.

Investigations are done to exclude organic causes:

- Stool analysis & culture.
- Sigmoidoscopy & rectal biopsy: *in cases of persistent diarrhea.*

TREATMENT

1. Psychotherapy: *reassurance* & *tranquillizers*.
2. Symptomatic:
   - For constipation: high-fibre diet & laxatives.
   - For diarrhea: loperamide.
   - For pain: antispasmodics.

CONSTIPATION

ETIOLOGY

1. Dietary factors:

- Lack of fibre and / or fluid intake.

2. Motility disorders:

- IBS.
- Drugs: Opiates, iron preparations, Aluminium containing antacids.
- Prolonged bed rest, myxoedema, paralytic ileus, ↑ Ca, ↓ K.

3. Structural disorders:

- Diverticular disease.
- Cancer colon.

4. Defecation problems:

- Simple constipation.
- Foecal impaction.
- Anal fissure.

5. Others:

- TB peritonitis.
- Typhoid fever.
- Anal fissure.

DYSPEPSIA

DEFINITION

- It is a non – specific term used to describe any abdominal discomfort ***related to meals***.
- It is also called indigestion.
- Dyspepsia includes a **variety of symptoms**:
  - Abdominal discomfort.
  - Bloatedness (faltulence).
  - Early satiety.
  - Epigastric fullness.
  - Epigastric pain.
  - Eructation or belching.
  - Heart burn.
  - Nausea with or without vomiting.

ETIOLOGY

I. Functional:

- No established organic cause.
- Mostly psychological.

II. Organic:

1) Almost all GIT & hepatobiliary diseases can cause dyspepsia …. e.g.
   - Oesophagus: oesophagitis & cancer oesophagus.
   - Stomach: peptic ulcer & cancer stomach.
   - Duodenum: duodenal ulcer.
   - Small intestine: enteritis & lymphoma.
   - Colon: colitis & cancer colon.
   - GB: cholecystitis & stones.
   - Liver: hepatitis & cirrhosis.
   - Pancreas: pancreatitis & cancer pancreas.

2) Extra – intestinal – diseases can cause dyspepsia …. e.g.
   - Right sided HF.
   - CRF.
   - Malignancy.
   - DRUGS ……e.g. NSAIDs.

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